Tetrahedron: Asymmetry Vol. 1, No. 2, pp. 87-96, 1990
Printed in Great Britain

0957-4166/90 $3.00+.00
Pergamon Press plc

Enzymatic Preparation of the Enantiomers of Some 1-Phenyl-1-alkanols†

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(*Received* 5 *December* 1989)

Abstract: The acetates of racemic 1-phenyl-1-heptanol, 1-phenyl-1-octanol and 1-phenyl-1-nonanol were hydrolyzed by *Pseudomonas* lipase in 10% acetone-0.1 M phosphate buffer (pH 6.9) at 30°C. Due to remarkable differences in the rates of hydrolysis of the enantiomeric acetates, the reaction led to (*R*)-(+)-alcohols (92.2-97.8% e.e.) and (*S*)-(-)-acetates (99.6-100.0% e.e.). Slow reverse esterification of 1-phenyl-1-octanol took place in the presence of 1 equivalent of acetic acid. Addition of ethyl acetate markedly increased the rate of esterification to give (*R*)-(+)-1-phenyloctyl acetate (92.8% e.e.). Attempts to esterify racemic alcohols in organic solvents were unsuccessful because of low reaction rate and/or low enantioselectivity.

INTRODUCTION

Enzymes — *vis vitalis* of the reactions in organisms — have proved to be excellent reagents *in vitro*. Hydrolases, especially lipases, have mostly been exploited due to remarkable enantioselectivity and low sensitivity to the changes in substrate structure with additional merits of requiring no coenzyme and having low cost. Quantitative evaluation of hydrolytic enzyme reactions by Sih and coworkers laid the basis for the applications of lipases and for the description of data as well.[1,2] The leading idea is to use enzymes under kinetic conditions, terminating the reaction at conversion less than 50% in order to prevent the decrease of the enantiomeric purity of the hydrolysis product. The common strategy of lipase application is screening among available lipases for the highest rate of conversion and the highest enantioselectivity under varia-

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†Preparative Bioorganic Chemistry ——XII. For Part XI, see Mori, K. and Chiba, N. *Liebigs Ann. Chem.* **1989**, 957.

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tions of temperature, composition of reaction media, and substrate structure.[3-5]

In general, a lipase preferentially hydrolyzes and esterifies the (*R*)-enantiomer of a substrate. The enantiomeric excess of the product is higher for a substrate with non-polar and more hydrophobic structure.[4,5] There is an indication that substituents at the α-position of the alcohol framework increase the enantioselectivity.[3,5] The hydrolysis reaction with a lipase, as a rule, is performed in a phosphate buffer at pH 7, and after the pH is kept constant in order to make the reaction irreversible.[3-6]

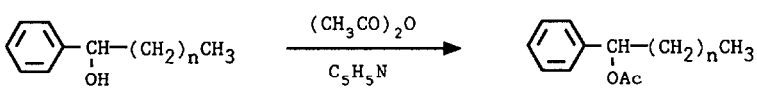
Recently, a considerable attention is being paid to lipase-catalyzed esterification or transesterification in organic media.[7-12] The reaction is performed in a neutral apolar organic media using the following systems: acid-alcohol,[7] acid anhydride-alcohol,[8,11] ester-alcohol,[9] and enol ester-alcohol.[9-12] The last system prevents the reverse reaction. In transesterification reaction, vinyl esters react faster than ethyl esters. Generally, lipase transesterification reaction in organic media is approximately ten times slower than hydrolysis reaction in aqueous media.[12]

Although the commercial lipases contain only a small amount of the active enzyme, partial purification of *Pseudomonas* lipase (lipase P) did not increase the enantiomeric purity of the product of esterification reaction.[8]

We became interested in resolving 1-aryl-1-alkanols employing lipases, because 1-aryl-1-alkanols with a lengthy alkyl chain might be useful in liquid crystal technology. Previous works on the enzymatic resolution of racemic 1-aryl-1-alkanols were restricted to only those with a shorter alkyl chain. Thus, 1-phenyl-1-ethanol,[7,11] 1-phenyl-1-propanol,[11] and 1-(2-halophenyl)-1-ethanols[10] were esterified in organic media by lipase P with almost complete enantioselection.

RESULTS AND DISCUSSION

Three 1-phenyl-1-alkanols, **1a**, **1b** and **1c** and the corresponding acetates **2a**, **2b** and **2c** were prepared in the conventional manner by the Grignard reaction followed by acetylation.



1a n=5
b n=6
c n=7

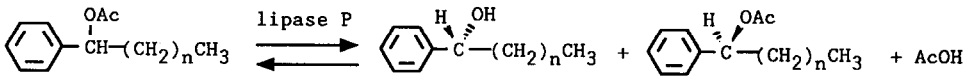
2a n=5
b n=6
c n=7

Among nine commercially available lipases and pig liver esterase (PLE), lipase P, *Candida cylindracea* (CC) lipase and PLE were quite

active in hydrolyzing **2b** in 0.1 M phosphate buffer (pH 7).

We first examined the reaction in organic solvents, benzene and heptane, employing lipase P as catalyst. Transesterification with vinyl and 2-propenyl acetates proceeded extremely slowly. Even after 90 hr, the content of the resulting ester was 25% and 10%, respectively. Caprylic acid in heptane gave no esterification at all. Esterification with acetic anhydride in heptane proceeded rather smoothly: after 30 hr, the content of the acetate was 46%, but the product and the remaining substrate were of very low enantiomeric purity (≤11% e.e.). Lipase CC and PLE in this reaction showed low rate of esterification: after 96 hr, the content of the ester was less than 21%. Transesterification as well as esterification in organic media thus did not seem to be promising, and we turned to the use of aqueous media.

The results in aqueous media are summarized in Table 1. Hydrolysis of the acetate (±)-**2b** by *Bacillus subtilis* var. *niger* slowly produced an alcohol (*R*)-(+)-**1b** of high enantiomeric purity and an acetate (*S*)-(-)-**2b** of low enantiomeric purity. Hydrolysis of (±)-**2b** by lipase CC in 10% acetone-0.1 M phosphate buffer (pH 6.9) at 30°C was very slow, and yielded the products of low enantiomeric purity. PLE in the same conditions showed moderate rate, and produced (*R*)-(+)-**1b** and (*S*)-(-)-**2b** of high enantiomeric purity.



(±)-2a n=5 b n=6 c n=7 (*R*)-(+)-1a n=5 b n=6 c n=7 (*S*)-(-)-2a n=5 b n=6 c n=7

Lipase P performed best of all, giving alcohol (*R*)-(+)-**1b** of the highest enantiomeric purity. With increase of the reaction time, the enantiomeric purity of the remaining acetate (*S*)-(-)-**2b** increased steadily, after 90 hr reaching 99.6% e.e. This e.e. value was based on the e.e. of (*S*)-(-)-**1b** obtained by treating (*S*)-(-)-**2b** with potassium carbonate in methanol. Potassium hydroxide in ethanol caused partial racemization.

(±)-1-phenylheptyl acetate (**2a**) and (±)-1-phenylnonyl acetate (**2c**) were hydrolyzed by lipase P in a similar manner giving (*R*)-(+)-**1a** and **1c** of >92% e.e. After 160 hr of the reaction period, the enantiomeric purity of (*S*)-(-)-**2a** and **2c** reached 100.0%. When they were treated with potassium carbonate in methanol, the resulting alcohols (*S*)-(-)-**1a** and **1c** showed no sign of the presence of their antipodes by HPLC analysis on a Chiralcel® OB column. The rate of the reaction was slowing down with increase of the enantiomeric purity of the remaining acetates, (*S*)-(-)-**2a** and **2c**. The (*S*)-configuration of the alcohol (-)-**1c** was confirmed by its

Table 1. Asymmetric hydrolysis of 1-phenylalkyl acetates (2a-c) in aqueous solutions

Substrate	Hydrolyzing agent	Reaction time, h	Conversion, % [a]	Specific rotation and enantiomeric purity of (*R*)-(+)-1			Specific rotation of (*S*)-(-)-2		Specific rotation and enantiomeric purity of (*S*)-(-)-1 from (*S*)-(-)-2		
				$[\alpha]_D^{25.}$	c [b]	e.e.,% [c]	$[\alpha]_D^{25.}$	c [b]	$[\alpha]_D^{25.}$	c [b]	e.e.,% [c]
2a	lipase P	5	21.8	+19.70	1.705	98.7	-20.27	1.715			
2a	lipase P	25	35.7	+19.85	1.795	99.4	-62.62	2.470			
2a	lipase P	120	39.8	+19.61	2.365	96.7	-71.40	2.050			
2a	lipase P	160	41.8	+19.16	2.765	92.2	-72.29	1.320	-20.54	0.88	100.0
2b	*B. subtilis*	138	30.0	+16.53	5.170		-24.76	5.280			
2b	lipase CC	167	36.0	+12.75	1.620		-27.82	1.620			
2b	PLE	46	47.1	+15.08	2.460		-53.48	3.140	-15.21	0.785	
2b	lipase P	5	13.7	+17.34	0.855	97.8	-11.71	2.725			
2b	lipase P	27	40.7	+17.24	1.475	99.4	-45.07	1.685			
2b	lipase P	72	50.1	+17.13	0.825	98.3	-59.19	2.890			
2b	lipase P	90	50.4	+17.24	1.260	97.8	-66.51	3.950	-18.13	3.03	99.6
2c	lipase P	5	23.6	+15.99	2.730	99.2	-12.41	3.040			
2c	lipase P	15	32.9	+16.33	1.560	99.4	-29.72	1.640			
2c	lipase P	147	53.1	+16.22	3.095	97.8	-62.56	2.180	-16.52	1.565	
2c	lipase P	160	49.5	+16.23	2.620		-62.99	3.070	-16.64	1.855	100.0
2c	lipase P	5	15.4	+16.39	0.800	99.0	-10.88	1.650			
2c	lipase P	25	43.9	+15.88	1.350	97.8	-44.66	1.290			
2c	lipase P	120	52.6	+15.42	1.730	97.4	-63.38	1.575	-15.69	0.775	98.0
2c	lipase P	167	61.4	+15.04	1.560	94.2	-63.57	1.565	-15.87	0.460	100.0

a) Determined by GC. b) In 99.5% ethanol solution.
c) Determined by HPLC on a Chiralcel® OB column.

oxidation with ruthenium tetraoxide[14] followed by reduction to give (*S*)-(-)-1,2- decanediol.[15]

It seemed that only the hydrolytic reaction was taking place. There was no contradiction, however, for the reverse esterification reaction to take part. Indeed, alcohol (±)-**1b** in the presence of lipase P was very slowly esterified with 1 equivalent of acetic acid under the normal reaction condition: after 44 hr, there was 0.37% of the acetate **2b**, and after 92 hr, 1.2%. We tried to increase the rate of esterification reaction in aqueous solutions by adding acetic acid, or changing the phosphate buffer to acetate buffer, or adding vinyl or ethyl acetate. The highest rate for esterification of **1a** was observed in acetate buffer (pH 5.2) in the presence of a large excess of ethyl acetate: after 24 hr of the reaction, 4.6% of the ester (*R*)-(+)-**2a** was found in the reaction mixture with enantiomeric purity of 92.8% (based upon specific rotation value).

Finally, to prove the large difference in the rate of enzymatic hydrolysis for (*R*)- and (*S*)-enantiomers of the acetate **2c**, they were separately subjected to hydrolysis catalyzed by lipase P under the normal reaction conditions. The results are shown in Table 2. (*R*)-Acetate **2c** was hydrolyzed with moderate rate. After 141 hr, almost all (*R*)-(+)-**2c** disappeared. Perhaps the remaining acetate was the contaminating (*S*)-**2c**, which originated from the not entirely 100% pure (*R*)-**1c** used for the preparation of the substrate (*R*)-**2c**. (*S*)-Acetate **2c**, to the contrary, remained nearly intact. Its exposure to lipase P over 171 hr resulted in less than 1% conversion.

Table 2. Hydrolysis of (*R*)-(+)- and (*S*)-(-)-**2c** with lipase P

Substrate	Reaction time (hr)	2	5	25	141	170
(*R*)-(+)-**2c**	Content of the	15.0	24.5	75.0	99.0	99.1
(*S*)-(-)-**2c**	alcohol (%)	0.06	0.00	0.15	0.80	0.82

The total enzymatic process catalyzed by lipase can be expressed in the following way:

$$\text{Enzyme} + (R)\text{-Acetate} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} (R)\text{-Alcohol} + CH_3CO_2H + \text{Enzyme}$$

$$\text{Enzyme} + (S)\text{-Acetate} \underset{k_4}{\overset{k_3}{\rightleftharpoons}} (S)\text{-Alcohol} + CH_3CO_2H + \text{Enzyme}$$

An ideal enzymatic resolution would give both (*R*)-alcohol and (*S*)-acetate in enantiomerically pure state. The substrate must then be only

one enantiomer. The reaction may require a considerably long time, because the rate will decrease with the decrease in the amount of the substrate. This in turn demands large differences between the forward and reverse reaction rate constants and between forward reaction rate constants of the both enantiomers ($k_1 \gg k_2$, $k_1 \gg k_3$).

The enzymatic hydrolysis reaction proceeds through the same transition state as that of the reverse esterification reaction. The forward reaction is first order (water is in excess), while the reverse reaction is a second order one. The reaction in a dilute solution can suppress the reverse reaction, and make $k_1 \gg k_2$. The rate of the reverse reaction may be decreased due to the binding of the liberated acetic acid to the basic groups of the enzyme protein.

Highly enantioselective enzymatic hydrolysis can be achieved after considerable time, reaching equilibrium state. Then the enantiomeric purity of the remaining (*S*)-acetate will not exceed $(k_1-k_2)/k_1$. An increase of the rate constants of the reverse (k_2) and competing forward (k_3) reactions would necessitate a longer reaction time to reach the equilibrium, and lead to possible decreased enantiomeric purity of the ester and the alcohol. The ratio k_1/k_3 determines the enantiomeric purity of the (*R*)-alcohol, while the ratio k_1/k_2 determines that of the remaining (*S*)-acetate.

CONCLUSIONS

Long chain (±)-1-phenylalkyl acetates **2a-c** were hydrolyzed by lipase P in 10% acetone-0.1 M phosphate buffer (pH 6.9-7.0) to give enantiomerically quite pure alcohols (*R*)-**1a-c** along with acetates (*S*)-**2a-c** of high enantiomeric purity after a long reaction period. Nearly exclusively the (*R*)-acetate was the substrate for the enzyme. This is the case of the large difference between the rate constants k_1 and k_2 as well as k_1 and k_3.

We propose the following procedure for the resolution of the racemic acetates **2a-c**: subject the racemic acetate to lipase hydrolysis for 100 hr, separate the (*R*)-alcohol from the remaining (*S*)-acetate, and the alcohol should be reacetylated and subjected again to the enzymatic hydrolysis.

Readily accessible enantiomerically pure 1-phenyl-1-alkanols may find application as new chiral starting materials in preparative organic chemistry.

EXPERIMENTAL

^{1}H NMR spectra were recorded on JEOL JNM FX-100 spectrometer at 100

MHz with $CHCl_3$ or TMS as an internal standard. IR spectra were measured as film on JASCO IRA-102 spectrometer. Optical rotations were measured on JASCO DIP 140 polarimeter in 99.5% ethanol solution. Merck Kieselgel 60 was used for SiO_2 column chromatography. Enantiomeric purity was determined by HPLC with Shimadzu LC-6A pump and Shimadzu SPD-6A spectrophotometric detector on Chiralcel® OB chiral column at 225 nm wavelength, solvent: hexane:THF:isopropyl alcohol=500:5:2.5. Gas chromatography (GC) was performed with Shimadzu GC-9A instrument at 200°C with polyethyleneglycol (10%) column. All compounds were purified by column chromatography, and the purity was checked by TLC (precoated glass plates, Merck Kieselgel F_{254}).

Due to minor differences in structure, all alcohols **1a-c**, racemic and optically active, have nearly the same spectral data: ^{1}H NMR δ 0.87 (3H, deformed t, *J*=7 Hz, $CH_2C\underline{H}_3$), 1.27 (br.s, $C\underline{H}_2$), 1.65-2.00 (2H, m, $HOCHC\underline{H}_2$), 1.87 (1H, s, O<u>H</u>), 4.66 (1H, t, -C<u>H</u>=, *J*=6.4 Hz), 7.35 (5H, s, $C_6\underline{H}_5$). IR ν 3370 (s), 2950 (s), 2870 (s), 1600 (w), 1490 (m), 1450 (s), 1380 (m), 1200 (m), 1110 (m), 1140 (s), 910 (m), 760 (s), 700 (s) cm^{-1}.

Spectral data of acetates **2a-c**: ^{1}H NMR δ 0.86 (3H, deformed t, *J*=7 Hz, $CH_2C\underline{H}_3$), 1.26 (s, $C\underline{H}_2$), 1.6-2.0 (2H, m, $=CHC\underline{H}_2$), 2.07 (3H, s, $COC\underline{H}_3$), 5.73 (1H, t, -C<u>H</u>=, *J*=6.9 Hz), 7.29 (5H, s, $C_6\underline{H}_5$). IR ν 2950 (s), 2870 (m), 1740 (s), 1490 (w), 1450 (m), 1370 (m), 1240 (s), 1110 (m), 950 (m), 760 (m), 600 (s) cm^{-1}.

Synthesis of starting 1-phenyl-1-alkanols 1a-c and their acetates 2a-c.

Freshly distilled benzaldehyde was subjected to Grignard reaction with alkylmagnesium bromides in dry ether or THF according to the common procedure to give **1a**: n_D^{25} 1.4931; **1b**, n_D^{25} 1.4915; **1c** n_D^{25} 1.4916.

Alcohols **1a-c** were treated with Ac_2O-C_5H_5N to give acetates **2a**: n_D^{25} 1.4754; **2b**, n_D^{25} 1.4755; **2c** n_D^{25} 1.4768.

General procedure for the enzymatic esterification of alcohol 1b in organic solvents.

The alcohol substrate (1 mmol) and esterifying reagent (enol ester, acetic anhydride or acid - 1 mmol) were dissolved in heptane or benzene (3 mL), lipase P (21 mg) and dry molecular sieves 4A (250 mg) were added. The mixture was incubated at 37°C in a shaker. The reaction was monitored by GC. After proper conversion was reached, the reaction mixture was filtered, the organic solution was washed with sat. sodium hydrogen carbonate solution, dried ($MgSO_4$) and concentrated. The residual oil was chromatographed over silica gel with hexane-ether mixture (50:1 to 20:1). Their structures and purities were checked as described above.

Microbial hydrolysis of acetate 2b.

Hydrolysis was performed according to ref. 13. *Bacillus subtilis* var. *niger* was cultured for 24 hr at 30°C in a nutrient broth [100 mL containing beef extract (0.33 g), peptone (1.11 g) and NaCl (0.56 g)]. Then substrate **2b** (ca 1 g) was added and the culture medium was shaken at 30°C. The course of reaction was periodically checked by GC. After 96 hr alcohol content reached 25.0%, after 140 hr - 27.2% and the reaction was stopped. The broth was extracted with ether. The ether extract was washed with brine, dried ($MgSO_4$) and concentrated. The residual oil (860 mg) was chromatographed over silica gel with *n*-pentane-ether (30:1) to give (*S*)-(-)-**2b** and, later, (*R*)-(+)-**1b**.

Enzymatic hydrolysis of the acetates 2a-c in phosphate buffer.

The following procedure is representative.

Acetate **2b** (248 mg, 1 mmol) was dissolved in acetone (5mL), the solution was added to 0.1 M phosphate buffer pH 6.9 (45 mL) along with 2 drops of Triton X-100. The suspension was homogenized and lipase P (250 mg) was added. The reaction mixture was shaken at 30°C for 5 hr. The content of alcohol **1b** reached 13.7% (GC). Ethyl acetate (10 mL) was added, mixture was shaken and hexane (20 mL) was added. All the mixture tended to jellify. The organic layer (containing some jelly) was separated. Into aqueous mixture solid NaCl was added and it was extracted with hexane-ethyl acetate (4:1) solvent system (3x30 mL). The combined organic layers were washed with brine (2x50 mL), sat. sodium hydrogen carbonate solution (3x50 mL), with brine again and dried ($MgSO_4$). Concentration gave a colorless oil (280 mg), which was purified by column chromatography, eluent: hexane-ether=50:1 to 15:1, to give alcohol (*R*)-(+)-**1b** (29.8 mg) and ester (*S*)-(-)-**2b** (210 mg).

According to this procedure were prepared enantiomerically pure alcohols: (*R*)-(+)-**1a**, n_D^{25} 1.4934 (Found: C, 80.82; H, 10.46. $C_{13}H_{20}O$ requires: C, 81.20; H, 10.48%); (*R*)-(+)-**1b**, n_D^{25} 1.4913 (Found: C, 81.50; H, 10.57. $C_{14}H_{22}O$ requires: C, 81.50; H, 10.75%); (*R*)-(+)-**1c**, n_D^{25} 1.4916 (Found: C, 81.48; H, 11.01. $C_{15}H_{24}O$ requires: C, 81.76; H, 10.98%),- and acetates: (*S*)-(-)-**2a**, n_D^{25} 1.4751 (Found: C, 76.57; H, 9.48. $C_{15}H_{22}O_2$ requires: C, 76.88; H, 9.46%); (*S*)-(-)-**2b**, n_D^{25} 1.4752 (Found: C, 77.08; H, 9.76. $C_{16}H_{24}O_2$ requires: C, 77.37; H, 9.74%); (*S*)-(-)-**1c**, n_D^{25} 1.4763 (Found: C, 77.34; H, 9.98. $C_{17}H_{26}O_2$ requires: C, 77.82; H, 9.99%).

Conversion of the acetates (S)-(-)-2a-c to (S)-(-)-1a-c.

The following procedure is representative.

Acetate (*S*)-(-)-**2a** (100 mg, 0.38 mmol) was dissolved in methanol (2 mL) and potassium carbonate (60 mg, 0.48 mmol) was added. The suspension

was stirred at room temp for 24 hr. The reaction mixture was diluted with ether, the solids were filtered, the solution was concentrated and the residue (ca 100 mg) was purified by column chromatography (eluent: hexane-ether=20:1). The product was dried in vacuum: (*S*)-(-)-**1a**, n_D^{25} 1.4933 (Found: C, 80.94; H, 10.39. $C_{13}H_{20}O$ requires: 81.20; H, 10.48%).

According to this procedure were prepared other (-)-alcohols: (*S*)-(-)-**1b**, n_D^{25} 1.4911 (Found: C, 81.04; H, 10.69. $C_{14}H_{22}O$ requires: 81.50; H, 10.75%); (*S*)-(-)-**1c**, n_D^{25} 1.4912 (Found: C, 81.45; H, 10.99. $C_{15}H_{24}O$ requires: C, 81.76; H, 10.98%).

Enzymatic esterification of 1a in acetate buffer.

Racemic 1-phenyl-1-heptanol **1a** (490 mg, 2.5 mmol) was dissolved in acetone (12 mL), the solution was added to 0.1 M sodium acetate solution (115 mL), along with 4 drops of Triton X-100, lipase P (500 mg) and acetic acid (0.2 mL). The mixture (pH 5.2) was shaken at 30°C for 18 hr. The content of the ester reached 0.32% (GC). Then ethyl acetate was added and the mixture was shaken at 30°C for further 24 hr. The amount of ester increased to 4.6% (GC). After workup, a crude colorless oil was chromatographically purified (eluent: hexane-ethyl acetate=25:1) to give acetate (*R*)-(+)-**2a** (25 mg): n_D^{25} 1.4752.

Enzymatic esterification of 1b in phosphate buffer.

Racemic 1-phenyl-1-octanol **1b** (206 mg, 1 mmol) was dissolved in acetone (5 mL) and added to 0.1 M phosphate buffer, pH 6.9 (45 mL) along with 1 drop of Triton X-100, lipase P (250 mg) and acetic acid (60 mg, 1 mmol). The mixture was shaken at 30°C. The amount of ester **2b** (GC) after 44 hr was 0.4%, after 92 hr - 1.2%, after 141 hr - 1.0%.

Conversion of (-)-1c to (S)-(-)-1,2-decanediol.

Acetic anhydride (0.3 mL) was added to a solution of (-)-**1c** [130 mg, 0.57 mmol, $[\alpha]_D^{25}$ -16.54° (EtOH)] in pyridine (0.5 mL). The mixture was left to stand overnight at room temp and worked up as usual to give 158 mg (quantitative) of crude **2c**. Ruthenium(III) chloride hydrate (5 mg) was added to a mixture of crude **2c** (158 mg), sodium periodate (2.0 g), carbon tetrachloride (2 mL), acetonitrile (2 mL) and water (3 mL). The mixture was stirred for 2 days at room temp, then diluted with water, and extracted with ether. The ether extract was washed with brine, dried ($MgSO_4$), and concentrated to give crude 2-acetoxydecanoic acid (161 mg). This acid in THF (2 mL) was added dropwise to lithium aluminum hydride (150 mg) in THF (8 mL) under ice-cooling. After stirring overnight at room temp, the mixture was worked up as usual to give crude 1,2-decanediol. This was purified by silica gel chromatography and recrystalli-

zation from *n*-hexane-ether to give 59 mg (57% from 1c) of (*S*)-1,2-decanediol, m.p. 47.0-47.5°C; $[\alpha]_D^{21}$ -13.8° (c=0.456, MeOH). lit.[15] m.p. 53-54°C; $[\alpha]_D^{22}$ -11.9° (c=0.431, MeOH). Its IR and ^{1}H NMR spectra were identical with those reported previously.[15]

Acknowledgement -- We thank Japan Cultural Association for a fellowship to R. B. and also for generous financial support of this work. Dr. S. Kuwahara's help in the determination of the absolute configuration of (-)-1c is acknowledged with thanks. Our thanks are due to Mr. M. Fujiwhara for typing the manuscript.

REFERENCES

1 Chen, C.-S.; Fujimoto, Y.; Girdaukas, G. and Sih, C. J. *J. Am. Chem. Soc.* **1982**, *104*, 7294.
2 Chen, C.-S.; Wu, S.-H.; Girdaukas, G. and Sih, C. J. *J. Am. Chem. Soc.* **1987**, *109*, 2812.
3 Scilimati, A.; Ngooi, T. K. and Sih, C. J. *Tetrahedron Lett.* **1988**, *29*, 4927.
4 Ngooi, T. K.; Scilimati, A.; Guo Z.-W. and Sih, C. J. *J. Org. Chem.* **1989**, *54*, 911.
5 Bianchi, D.; Cesti, P. and Golini, P. *Tetrahedron* **1989**, *45*, 869.
6 Faber, K.; Hoenig, H. and Seufer-Wasserthal, P. *Tetrahedron Lett.* **1988**, *29*, 1903.
7 Kirchner, G.; Scollar, M. P. and Klibanov, A. M. *J. Am. Chem. Soc.* **1985**, *107*, 7072.
8 Yamamoto, K.; Nishioka, T.; Oda, J. and Yamamoto, Y. *Tetrahedron Lett.* **1988**, *29*, 1717.
9 Terao, Y.; Murata, M.; Achiwa, K.; Nishio, T.; Akamatsu, M. and Kamimura, M. *Tetrahedron Lett.* **1988**, *29*, 5173.
10 Hiratake, J.; Inagaki, M.; Nishioka, T. and Oda, J. *J. Org. Chem.* **1988**, *53*, 6130.
11 Bianchi, D.; Cesti, P. and Battistel, E. *J. Org. Chem.* **1988**, *53*, 5531.
12 Wang, Y.-F.; Lalonde, J. J.; Momongan, M.; Bergbreiter, D. E. and Wong, C.-H. *J. Am. Chem. Soc.* **1988**, *110*, 7200.
13 Mori, K. and Akao, H. *Tetrahedron* **1980**, *36*, 91.
14 Carlsen, P. H. J.; Katsuki, T.; Martin, V. S. and Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936.
15 Masaoka, Y.; Sakakibara, M. and Mori, K. *Agric. Biol. Chem.* **1982**, *46*, 2319.