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Synthesis of Enantiomerically Enriched *anti*-Homoallyl Alcohols Mediated by Crude Chicken Liver Esterase (CCLE)

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Abstract: Enantiomerically enriched anti-homoallyl alcohols were synthesized in 67->99% enantiomeric purities via enantioselective hydrolysis of the corresponding racemic acetates mediated by Crude Chicken Liver Esterase (CCLE).

Biologically active molecules with multiple stereogenic centers such as macrolide (*e.g.*, rapamycin) and polyether (*e.g.*, ionomycin) antibiotics have been challenging synthetic targets for organic chemists mainly because such syntheses have to be both diastereo- and enantioselective.[1,2] In addition, syntheses of such structurally non-rigid complex molecules require stereochemically well-defined building blocks.

Diastereomerically and enantiomerically pure homoallyl alcohols have proved to be invaluable surrogates in the synthesis of molecules with multiple stereogenic centers.[3,4] This is because of the versatility of homoallyl alcohols *i.e.*, they can be converted into aldols, epoxides, lactones, *etc.* with great ease. Owing to their immense potential, the diastereo- and enantioselective synthesis of homoallyl alcohols has generated a lot of interest and significant strides have been made in this area.[5] Still truly general and economical methods have yet to emerge. Moreover, most of the methods of practical importance require the source of chiral information in stoichiometric quantities.

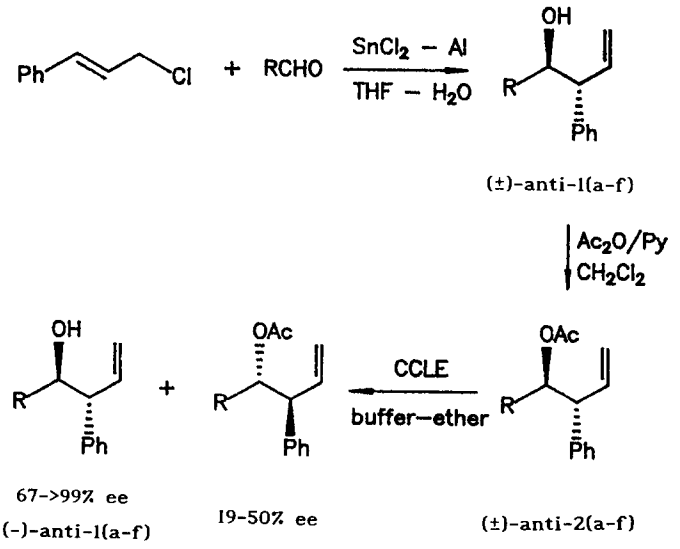
The biocatalytic approach has recently emerged as a major tool for the preparation of a variety of homochiral molecules.[6] Normally pure isolated enzymes or whole cells have been used for this purpose. We[7] and several others[8] have shown that the use of crude preparations of certain enzymes as substitutes for the original pure enzymes is as good as using

the isolated pure ones. We have quite successfully utilized acetone powders of livers from porcine,[9] goat,[10] bovine[11] and chicken[12] in the resolution of various racemic secondary alcohols as attractive substitutes for the original esterases. We herein report the highly enantioselective hydrolyses of acetates of racemic *anti*-homoallyl alcohols mediated by crude chicken liver esterase (CCLE, as liver acetone powder) that produced the desired alcohols with good to high enantiomeric purities.

Results and discussion :

The racemic *anti*-homoallyl alcohols **1a-1f** were prepared following the procedure reported by Torii *et al.*[13] from cinnamyl chloride and corresponding aldehydes using zero valent tin (from $SnCl_2$-Al) as the metal. These alcohols were converted into the corresponding acetates **2a-2f** by treatment with acetic anhydride in the presence of pyridine. These racemic acetates **2a-2f** were then subjected to crude chicken liver esterase (CCLE) mediated enantioselective hydrolysis in a biphasic medium consisting ether and 0.5 M, pH 8.0, phosphate buffer in 1:4 ratio at room temperature. This hydrolyses resulted in the production of desired (-)-alcohols in 67->99% enantiomeric purities and enantiomerically enriched unhydrolyzed acetates in 19-50% ee (Scheme 1, Table 1).

SCHEME 1 :



R = a) isopropyl, b) isobutyl, c) n-butyl, d) n-pentyl, e) n-hexyl, f) phenyl

Table 1: Crude Chicken Liver Esterase (CCLE) Catalyzed Enatioselective Hydrolysis of (±)-*anti*-4-Acetoxy-3-phenylalkenes[a]:

Substrate  2a-2f(R=)	Time in hrs.	Conversion Ratio[c] OH:OAc	(-)-Alcohol[b]			Recovered acetate		E[h]
			Yield[d] %	$[\alpha]_D^{20}$[e] (chloroform)	ee[f] %	Yield[d] %	ee[g] %	
iPr(2a)	264	25:75	22	- 60.6(c 1.12)	67	69	19	6
iBu(2b)	75	32:68	29	- 47.2(c 2.20)	>99	65	49	316
nBu(2c)	65	22:78	20	- 57.4(c 1.55)	90	72	24	24
nPent(2d)	75	35:65	31	- 51.6(c 1.61)	94	61	50	53
nHex(2e)	144	35:65	30	- 47.8(c 2.18)	93	60	49	45
Ph(2f)	240	25:75	20	- 13.3(c 1.12)	94	69	25	44

a) All reactions were carried out in 5 mM scale with 2g of CCLE.

b) Diastereomeric composition (*syn:anti*) of (-)-alcohols:
1a: 2:98, **1b:** 3:97, **1c:** 3:97, **1d:** 2:98, **1e:** 2:98, **1f:** 2:98.

c) Determined by HPLC analysis.

d) Yields are of column purified products.

e) Optical rotations of all compounds were recorded in chloroform.

f) Determined by ^{1}H NMR (200 MHz) analysis of corresponding acetates in presence of chiral shift reagent, Eu(hfc)$_3$ and refer to only that of *anti*-isomer.

g) Determined by ^{1}H NMR (200 MHz) analysis in presence of chiral shift reagent, Eu(hfc)$_3$ and refer to only that of *anti*-isomer.

h) Calculated using the Sih equation.[14]

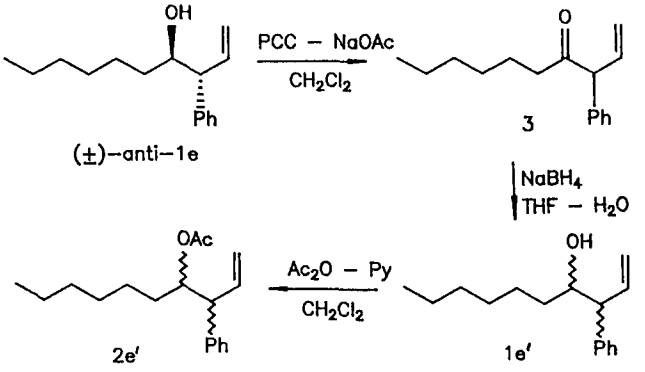
Determination of diastereomeric purity of the alcohols **1a-1f** :

The diastereomeric purity of the alcohols **1a-1f** was established by ^{1}H NMR (200 MHz) analysis of the corresponding acetates as described in the following. Invariably the ^{1}H NMR spectra of all the racemic acetates (±)-**2a-2f** contained one singlet with very low intensity at upfield (δ 2.00 - 1.80) in addition to the original methyl signal of acetoxy group.[15] This low intense singlet was attributed to the methyl signal of acetoxy group of minor *syn*-diastereomer and was confirmed in the case of acetate **2e** as follows.

The ^{1}H NMR spectrum of the racemic acetate **2e** showed two singlets for the methyl protons of acetoxy group at δ 2.04 and 1.86 in 94:6 ratio. Then the corresponding racemic alcohol **1e** was oxidized to the ketone **3**

using pyridinium chlorochromate buffered with sodium acetate. The ketone **3** was reduced with sodium borohydride to furnish the alcohol **1e'** which was as such converted into the corresponding acetate **2e'** (Scheme 2). The ^{1}H NMR spectrum of the acetate **2e'** showed two singlets at δ 2.04 and 1.86 in the ratio 22:78 indicating that the acetate **2e'** contained *syn*-diastereomer in excess where as the acetate **2e** has the *anti*-isomer in excess.

SCHEME 2 :



Based on the above observation, the ratios of the two singlets of methyl protons of acetoxy group in the ^{1}H NMR spectra of the acetates **2a-2f** was taken as the diastereomeric composition of the corresponding alcohols **1a-1f** (refer to experimental). It was also observed that the *anti*-acetates were hydrolysed faster by CCLE compared to *syn*-acetates as indicated by the increased diastereomeric purities of (-)-alcohols (Table 1).

Determination of enantiomeric purity:

The enantiomeric purities of all the (-)-alcohols were determined by the ^{1}H NMR (200 MHz) analysis of corresponding acetates in presence of chiral shift reagent, Eu(hfc)$_3$ using same analysis of the corresponding racemic acetate as the reference in each case. The recovered acetates were also subjected to the same analysis to determine the enantiomeric enrichment.

Determination of absolute configuration of (-)-alcohols and recovered acetates :

The absolute configuration of (-)-*anti*-3,4-diphenylbut-1-en-4-ol **(1f)** was shown to be 3R,4S.[16] Therefore it is the (3R,4S)-*anti*-4-acetoxy-3,4-diphenylbut-1-ene **(2f)** that was hydrolyzed preferentially by CCLE. This

fact leads us to believe that CCLE exhibits preference to the acetates with configuration shown in FIG.1. Since the stereochemical specificities of enzymes could be used to establish the absolute stereochemistry of their substrates,[17,18] the absolute configurations of (-)-alcohols (-)-**1a-1e** were tentatively assigned as 3R,4R (note the change in priorities of groups) and that of recovered acetates as 3S,4S. This has been further supported by the similar behavior (relative shift differences) of all the acetates of (-)-alcohols (major peak of separated acetoxy-methyl protons signals appears in upfield) and exactly opposite behavior of the corresponding recovered acetates (major peak of separated acetoxy-methyl protons signals appears in downfield) during their ^{1}H NMR analysis in the presence of chiral shift reagent, $Eu(hfc)_3$.[19]

(3R,4S)-2f (3R,4R)-2(a-e)

FIGURE 1.

Conclusion :

This paper describes simple enantioselective synthesis of alcohols (-)-**1a-1f**. As it should be possible to get homochiral molecules by controlling percentage of conversion or by resubmitting the acetates of enantiomerically enriched alcohols,[20,21] our methodology offers an easy access to homochiral *anti*-homoallyl alcohols. In summary we have shown that CCLE is an economical and suitable enzyme system for the preparation of enantiomerically enriched *anti*-homoallyl alcohols.

Experimental :

Boiling points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 1310 or 297 spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded either on JEOL-FX-100 (100 MHz) or Bruker 200 (200 MHz) spectrometer using chloroform-d as solvent and TMS as internal reference. Elemental analysis was performed on a Perkin-Elmer 240C-CHN analyzer. HPLC analysis was carried out on a SHIMADZU LC-10AD equipped with SPD-10A UV-VIS detector using special grade solvents. Column chromatography was carried out using Acme's silica gel (100-200 mesh). Optical rotations were measured on Autopol II automatic polarimeter at the wave length of the sodium D-line (589 nm) and at 20 ^{o}C.

Crude Chicken Liver Esterase (CCLE) :

Freshly purchased chicken liver (500 g) was homogenized in chilled acetone (2 L) using kitchen juicer. The brown mass obtained after filtration was homogenized again with chilled acetone. The residue obtained after filtration was air dried at room temperature and powdered using juicer. The fibrous material was removed by sieving to afford 80-90 g of CCLE as fine powder. This powder (chicken liver acetone powder) can be stored in refrigerator for 2-3 months without any significant loss of activity.

(±)-*anti*-Homoallyl alcohols 1(a-f):

General procedure:

These compounds were prepared following literature procedure.[13]

To a mixture of cinnamyl chloride (11.1 mL, 80 mM) and aldehyde (100 mM) {in case of aliphatic aldehydes 3-5 equivalents) in THF (100 mL), water (40 mL) was added and the resulting suspension was heated to 60°C. Then aluminum powder (2.16 g, 80 mM) and tin (II) chloride dihydrate (9.02 g, 40 mM) were added in quick succession with vigorous stirring. Then the reaction mixture was stirred for 3h at 60°C. The reaction mixture was cooled to room temperature and diluted with 2N HCl (50 mL). The reaction mixture was extracted with ether (3 x 50 mL). The combined organic layer was washed with saturated $NaHCO_3$ solution and dried over anhydrous Na_2SO_4. Removal of solvent followed by column chromatography (silica gel, 10% ethyl acetate in hexane) of the crude afforded pure alcohol as a colorless liquid. The diastereomeric ratio of all the alcohols **1a-1f** was determined by the ^1H NMR (200 MHz) analysis of corresponding acetates **2a-2f**.

(±)-*anti*-5-methyl-3-phenylhex-1-en-4-ol (1a) : Yield : 73% IR (neat) : 3400 cm^{-1}, ^1H NMR (100 MHz): δ 0.80-1.04 (m, 6H), 1.32-1.96 (m, 2H, 1H D_2O washable), 3.16-3.64 (m, 2H), 4.92-5.28 (m, 2H), 5.84-6.32 (m, 1H), 6.96-7.40 (m, 5H). ^{13}C NMR (25 MHz): δ 15.76, 20.06, 29.70, 54.59, 78.47, 116.53, 126.59, 128.06, 128.77, 138.89, 142.18.
Anal. Calcd. for $C_{13}H_{18}O$: C, 82.05; H, 9.53. Found : C, 81.89; H, 9.51.

(±)-*anti*-6-Methyl-3-phenylhept-1-en-4-ol (1b): Yield: 72%, b.p. : 98-100°C at 1 mm, IR (neat) : 3425 cm^{-1}, ^1H NMR (100 MHz) : δ 0.80-1.02 (m, 6H), 1.00-1.96 (m, 4H, 1H D_2O washable), 3.20 (t, 1H, J = 8 Hz), 3.84 (m, 1H), 4.92-5.28 (m, 2H), 5.80-6.32 (m, 1H), 6.88-7.40 (m, 5H). ^{13}C NMR (25 MHz): δ 21.64, 23.76, 24.53, 43.88, 57.82, 72.18, 117.65, 126.71, 128.30, 128.77, 138.65, 142.18.

Anal. Calcd. for $C_{14}H_{20}O$: C, 82.30; H, 9.86. Found : C, 82.19; H, 9.83.

(±)-*anti*-3-Phenyloct-1-en-4-ol (1c): Yield: 74%, b.p : 116-118°C at 2 mm, IR (neat): 3350 cm^{-1}, ^1H NMR (100 MHz): δ 0.80 (distorted t, 3H), 1.30 (m, 6H), 1.72 (br, 1H, OH), 3.20 (t, 1H, J= 8 Hz), 3.72 (m, 1H), 4.92-5.24 (m, 2H), 5.84-6.28 (m, 1H), 6.92-7.36 (m, 5H) ^{13}C NMR (50 MHz): δ 13.91, 22.50 27.83, 34.16, 57.11 73.97, 117.36, 126.42, 127.99, 128.48, 138.34, 141.85.
Anal. Calcd. for $C_{14}H_{20}O$: C, 82.30; H, 9.86. Found : C, 82.18; H, 9.82.

(±)-*anti*-3-Phenylnon-1-en-4-ol (1d): Yield: 70%, b.p. : 110-112°C at 2 mm, IR (neat) : 3400 cm^{-1}, ^1H NMR (100 MHz): δ 0.84 (distorted t, 3H), 1.28 (m, 8H), 1.72 (br, 1H, OH), 3.20 (t, 1H, J = 7.5 Hz), 3.76 (m, 1H), 4.92-5.28 (m, 2H), 5.80-6.28 (m, 1H), 6.96-7.40 (m, 5H). ^{13}C NMR (25 MHz): δ 14.00, 22.59, 25.47, 31.82, 34.59, 57.23, 74.12, 117.53, 126.65, 128.34, 128.71, 138.59, 142.12
Anal. Calcd. for $C_{15}H_{22}O$: C, 82.51; H, 10.15. Found : C, 82.65; H, 10.09.

(±)-*anti*-3-Phenyldec-1-en-4-ol (1e): Yield: 74%, b.p.: 120-122 °C at 1 mm, IR (neat) : 3425 cm^{-1}, ^1H NMR (100 MHz): δ 0.84 (distorted t, 3H), 1.22 (m, 10H), 1.76 (br, 1H, OH), 3.20 (t, 1H, J = 8 Hz), 3.76 (m, 1H), 4.96-5.28 (m, 2H), 5.80-6.32 (m, 1H), 6.92-7.44 (m, 5H). ^{13}C NMR (25 MHz): δ 17.94, 22.47, 25.59, 29.11, 31.70, 34.41, 57.18, 74.00, 117.59, 126.53, 128.06, 128.65, 138.48, 141.94.
Anal. Calcd. for $C_{16}H_{24}O$: C, 82.70; H, 10.41. Found : C, 82.55; H, 10.44.

(±)-*anti*-3,4-Diphenylbut-1-en-4-ol (1f): Yield: (78%), IR (neat): 3375 cm^{-1}; ^1H NMR (100 MHz): δ 2.36 (br, 1H, OH), 3.44 (t, 1H, J = 8 Hz), 4.68 (d, 1H, J = 8 Hz), 4.88-5.22 (m, 2H), 5.84-6.34 (m, 1H), 6.96-7.36 (m, 10H). ^{13}C NMR (25 MHz): δ 58.94, 77.12, 118.18, 126.53, 126.71, 127.36, 127.89, 128.30, 137.94, 140.71, 142.01.
Anal. Calcd. for $C_{16}H_{16}O$: C, 85.67; H, 7.19. Found : C, 85.67; H, 7.18.

Acetates of (±)-*anti*-homoallyl alcohols 2 (a-f):

General procedure:

To a mixture of **(±)-1** (50 mM), pyridine (8.5 mL, 105 mM) and DMAP (0.24 g, 2 mM) in dry dichloromethane (50 mL), acetic anhydride (9.4 mL, 100 mM) was added slowly with stirring at room temperature. After stirring for 2 h, the reaction mixture was taken up in ether (75 mL) and washed successively with ice-cold 2N HCl (3 x 30 mL) and saturated K_2CO_3 solution. The organic layer was dried over anhydrous Na_2SO_4 and concentrated. The liquid obtained, was column purified (silica gel, 10 % ethyl

acetate in hexane) to afford pure racemic acetate as a colorless liquid

(±)-*anti*-4-Acetoxy-5-methyl-3-phenylhex-1-ene (2a): Yield: 92%, IR (neat): 1730 cm^{-1}, ^1H NMR (200 MHz) : δ 0.90 (two d, 6H, J = 6 Hz), 1.52-1.71 (m, 1H), 1.82 & 2.04 (two singlets in 3:97, 3H), 3.54 (t, 1H, J = 8 Hz), 5.05-5.25 (m, 3H), 5.90-6.15 (m, 1H), 7.20-7.40 (m, 5H). ^{13}C NMR (25 MHz): δ 15.42, 19.53, 20.58, 28.59, 52.88, 79.00, 116.18, 126.59, 127.77, 128.59, 138.53, 141.00, 170.47. Contains ≃3% *syn*-isomer.

(±)-*anti*-4-Acetoxy-6-methyl-3-phenylhept-1-ene (2b): Yield: 93% IR (neat): 1740 cm^{-1}, ^1H NMR (200 MHz): δ 0.82 (two doublets, 6H, J = 5 Hz) 1.05-1.65 (m, 3H), 1.86 & 2.04 (two singlets in 5:95, 3H), 3.35 (t, 1H, J = 8 Hz), 5.05-5.18 (m, 2H), 5.24-5.40 (m, 1H), 5.94-6.14 (m, 1H), 7.15-7.40 (m, 5H) ^{13}C NMR (25 MHz): δ 20.70, 21.29, 23.11, 24.29, 41.29, 55.71, 73.82, 116.36, 126.59, 127.89, 128.53, 138.24, 140.89, 170.11. Contains ≃5% *syn*-isomer.

(±)-*anti*-4-Acetoxy-3-phenyloct-1-ene (2c): Yield: 92% IR (neat): 1730 cm^{-1} ^1H NMR (200 MHz): δ 0.80 (m, 3H), 1.10-1.51 (m, 6H), 1.86 & 2.04 (two singlets in 6:94, 3H), 3.40 (t, 1H, J = 8 Hz), 5.02-5.30 (m, 3H), 5.90-6.12 (m, 1H), 7.22 (m, 5H). ^{13}C NMR (25 MHz): δ 13.29, 20.41, 21.76, 26.84, 31.41, 54.65, 75.24, 116.12, 126.36, 127.65, 128.24, 137.83, 140.65, 168.73. Contains ≃6% *syn*-isomer.

(±)-*anti*-4-Acetoxy-3-phenylnon-1-ene (2d): Yield: 94% IR (neat): 1730 cm^{-1} ^1H NMR (200 MHz) : δ 0.85 (distorted t, 3H), 1.12-1.50 (m, 8H), 1.88 & 2.05 (two singlets in 7:93, 3H), 3.40 (t, 1H, J = 8 Hz), 5.05-5.30 (m, 3H), 5.95-6.15 (m, 1H), 7.15-7.40 (m, 5H). ^{13}C NMR (25 MHz) : δ 13.82, 21.00, 22.35, 24.88, 31.41, 32.17, 55.12, 75.82, 116.65, 126.83, 128.12, 128.71, 138.30, 141.12, 170.77. Contains ≃7% *syn*-isomer.

(±)-*anti*-4-Acetoxy-3-phenyldec-1-ene (2e) : Yield : 94%, IR (neat) : 1740 cm^{-1}, ^1H NMR (200 MHz) : δ 0.85 (distorted t, 3H), 1.12-1.50 (m, 10H), 1.85 & 2.08 (two singlets in 6:94, 3H), 3.40 (t, 1H, J = 8 Hz), 5.05-5.30 (m, 3H), 5.90-6.20 (m, 1H), 7.15-7.40 (m, 5H). ^{13}C NMR (25 MHz) : δ 13.76, 20.76, 22.29, 25.06, 28.76, 31.41, 32.12, 55.06, 75.59, 116.47, 126.71, 128.01, 128.18, 128.59, 138.24, 141.00, 170.47. Contains ≃6% *syn*-isomer.

(±)-*anti*-4-Acetoxy-3,4-diphenylbut-1-ene (2f) : Yield : 92%, IR (neat): 1730 cm^{-1}, ^1H NMR (200 MHz) : δ 1.85 & 2.08 (two singlets in 3:97, 3H), 3.75 (t, 1H, J = 8 Hz), 5.05-5.26 (m, 2H), 5.91-6.30 (m, 2H), 6.87-7.40

(m, 10H); ^{13}C NMR (25 MHz): δ 21.11, 56.65, 78.35, 117.30, 126.83, 127.30, 127.89, 128.16, 128.48, 128.59, 137.77, 138.68, 140.01, 170.24. Contains ≃3% *syn*-isomer.

4-Oxo-3-phenyldec-1-ene (3):

To a stirred suspension of pyridinium chlorochromate (2.15 g, 10 mM) and sodium acetate (0.164 g, 2 mM) in dichloromethane (10 mL) was added racemic alcohol **1e** (0.46 g, 2 mM) in dichloromethane (2 mL) in one portion and stirring was continued for 3 h at room temperature. Usual workup provided the ketone **3** as a colorless liquid. Yield: 0.4 g (87%). IR (neat) : 1710 cm^{-1}. ^1H NMR (200 MHz) : 0.85 (distorted t, 3H), 1.12-1.65 (m, 8H), 2.45 (t, 2H, J = 6 Hz), 4.38 (d, 1H, J = 6 Hz), 5.00-5.28 (m, 2H), 6.15- 6.35 (m, 1H), 7.18-7.42 (m, 5H).

4-Acetoxy-3-phenyldec-1-ene (2e') (*mixture of diastereomers*) :

To a mixture of water (2 mL) and a solution of the ketone **3** (0.23 mg, 1 mM) in THF (2 mL) was added solid sodium borohydride (50 mg) carefully with stirring at room temperature. Stirring was continued for 30 min. and then dilute HCl (2 mL) was added to destroy the excess hydride. The reaction mixture was extracted with ether (3 x 5 mL) and combined ether layers was dried over anhydrous sodium sulphate. Removal of solvent gave pure alcohol **1e'** (0.19 g, 82%) which was converted into the corresponding acetate **2e'** following the procedure described previously. Yield : 0.18 g (82%). IR (neat) : 1740 cm^{-1}, ^1H NMR (200 MHz): δ 0.85 (m, 3H), 1.12-1.75 (m, 10H), 1.85 (*syn*) & 2.08 (*anti*) (two singlets in 78:22, 3H), 3.42 (*anti*) & 3.51 (*syn*) (two triplets, 1H), 5.05-5.34 (m, 3H), 5.92-6.14 (m, 1H), 7.15-7.40 (m, 5H).

CCLE-catalyzed hydrolysis of racemic acetates of *anti*-homoallyl alcohols 2(a-f) : *General procedure :*

To 0.5 M, pH 8.0, KH_2PO_4/K_2HPO_4 buffer (40 mL) racemic acetate (5 mM) in ether (10 mL) was added with stirring at room temperature. After 10 min., CCLE (2 g) was added and the stirring was continued. The progress of the hydrolysis was monitored by HPLC. When an appropriate degree of hydrolysis was accomplished, the reaction was quenched with 2N HCl (10 mL). To this sodium chloride (5g) and dichloromethane (50 mL) were added and the resulting suspension was vigorously stirred for 0.5 h Then the enzyme was removed by filtration with suction and the layers were separated. The aqueous layer was extracted with dichloromethane (3 x 20 mL). The combined organic layer was dried over anhydrous Na_2SO_4. Removal of solvent followed by column chromatography (silica gel, 10% ethyl acetate

in hexane) afforded (-)-alcohol and unhydrolyzed acetate.

Determination of enantiomeric purity — *General procedure* :

Enantiomeric purities were determined by ^{1}H NMR (200 MHz) analysis of the acetate (5 mg) of (-)-alcohol in presence of chiral shift reagent, Eu(hfc)$_3$ (progressive addition) with reference to racemic acetate (the singlet of acetoxy-methyl protons separate). The recovered optically active acetates were also subjected to same analysis.

CCLE-catalyzed hydrolysis of (±)-*anti*-4-acetoxy-5-methyl-3-phenylhex-1-ene (2a):

Hydrolysis of (±)-**2a** (1.16 g, 5 mM) with CCLE (2 g) in 11 days afforded (-)-alcohol and unhydrolyzed acetate in 25:75 ratio.
(-)-Alcohol : Yield : 0.21 g (22%), $[\alpha]_D^{20}$ - 60.6 (c 1.12, $CHCl_3$), 67% ee.
Recovered acetate : Yield : 0.8 g (69%). 19% ee.

CCLE-catalyzed hydrolysis of (±)-*anti*-4-acetoxy-6-methyl-3-phenylhept-1-ene (2b):

Hydrolysis of (±)-**2b** (1.23 g, 5 mM) with CCLE (2 g) in 75 hr afforded (-)-alcohol and unhydrolyzed acetate in 32:68 ratio.
(-)-Alcohol : Yield : 0.3 g (29%), $[\alpha]_D^{20}$ - 47.2 (c 2.20, $CHCl_3$), >99% ee.
Recovered acetate : Yield : 0.8 g (65%), 49% ee.

CCLE-catalyzed hydrolysis of (±)-*anti*-4-acetoxy-3-phenyloct-1-ene (2c):

Hydrolysis of (±)-**2c** (1.23 g, 5 mM) with CCLE (2 g) in 65 hr afforded (-)-alcohol and unhydrolyzed acetate in 22:78 ratio.
(-)-Alcohol : Yield : 0.2 g (20%), $[\alpha]_D^{20}$ - 57.4 (c 1.55, $CHCl_3$), 90% ee.
Recovered acetate : Yield : 0.88 g (72%), 24% ee.

CCLE-catalyzed hydrolysis of (±)-*anti*-4-acetoxy-3-phenylnon-1-ene (2d):

Hydrolysis of (±)-**2d** (1.3 g, 5 mM) with CCLE (2 g) in 75 hr afforded (-)-alcohol and unhydrolyzed acetate in 35:65 ratio.
(-)-Alcohol: Yield : 0.34 g (31%), $[\alpha]_D^{20}$ - 51.6 (c 1.61, $CHCl_3$), 94% ee.
Recovered acetate : Yield : 0.79 g (61%), 50% ee.

CCLE-catalyzed hydrolysis of (±)-*anti*-4-acetoxy-3-phenyldec-1-ene (2e):

Hydrolysis of (±)-**2e** (1.37 g, 5 mM) with CCLE (2 g) in 6 days afforded (-)-alcohol and unhydrolyzed acetate in 35:65 ratio.
(-)-Alcohol : Yield : 0.35 g (30%), $[\alpha]_D^{20}$ - 47.8 (c 2.18, $CHCl_3$), 93% ee.
Recovered acetate : Yield : 0.82 g (60%), 49% ee.

CCLE-catalyzed hydrolysis of (±)-*anti*-4-acetoxy-3,4-diphenylbut-1-ene (2f)

Hydrolysis of (±)-**2f** (1.33 g, 5 mM) with CCLE (2 g) in 10 days afforded (-)-alcohol and unhydrolyzed acetate in 25:75 ratio.
(-)-Alcohol : yield = 0.22 g (20%), $[\alpha]_D^{20}$ - 13.3 (c 1.12, $CHCl_3$), 94 % ee {lit.[16] $[\alpha]_D$ - 12.5 (c 3.4, $CHCl_3$), 97% ee, config. 3R,4S}.
Recovered acetate : Yield : 0.92 g (69%), 25 % ee.

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