Secondary alcohols having enantiomeric purity are important synthetic intermediates and are useful chiral auxiliaries in both synthetic and analytical chemistry applications *(J. Chem. Soc., Chem. Commun.* **1988,** 1459). Because of the wide applicability of secondary alcohols; there has been an interest and demand to synthesize them in enantiomerically pure form. Many methods have been reported in the literature based on enantioselective reduction of the corresponding ketones. *(Tetrahedron. Lett.* **2000,** *41,* 4135; *Tetrahedron: Asymmetry* **2000,** *11,* 3671). These include the use of chiral reducing agents, chiral boranes, chiral catalysts, enantioselective homogeneous hydrogenation, and the reduction employing the whole cells

We claim

1. An one-pot chemoenzymatic process for the stereoselective preparation of secondary alcohols from corresponding ketones which comprises

   e) reacting ketone (1) with a reducing agent in a molar ratio in the range of 1:1.5-1:2.5 in an organic solvent, at a temperature in the range of 30-50 °C for a period of 2-4 hrs,

   f) adding Lipase and an acetylating agent selected from isopropenyl acetate and vinyl acetate to the above said reaction mixture,

   g) stirring the above said reaction mixture for a period of 4-12 hrs, at a temperature of 20-30°C to obtain the corresponding recimic alcohol (2) and recemic acetate (3),

   h) reacting the above said recemic acetate (3) with potassium bicarbonate in an organic solvent, at a temperature of 20-30 °C for a period of 2-4 hrs to obtain the desired recemic alcohol (4)

2) A process as claimed in claim 1 wherein the ketone used is selected from the group consisting of acetophenone, propiophenone, 2-chloropropiophenone, 4-benzyloxy acetophenone, 4-allyloxy acetophenone and 4-nitro acetophenone

3) A process as claimed in claims 1&2, wherein the reducing agent used is sodium borohydride.

4) A process as claimed in claims 1-3, wherein the organic solvent used is selected from the group consisting of hexane, diisopropyl ether, t-butylmethyl ether, tetrahydrofuran and toluene.

5) A process as claimed in claims 1-4, wherein the lipase used is selected from the group consisting of *Pseudomonas cepacia* lipase (Amano PS), immobilized lipase PS-Amano C, PS-Amano D, and *Pseudomonas fluorescence.*

6) A process as claimed in claims 1-5, wherein the acetylating agent used is selected from vinyl acetate and isopropenyl acetate.

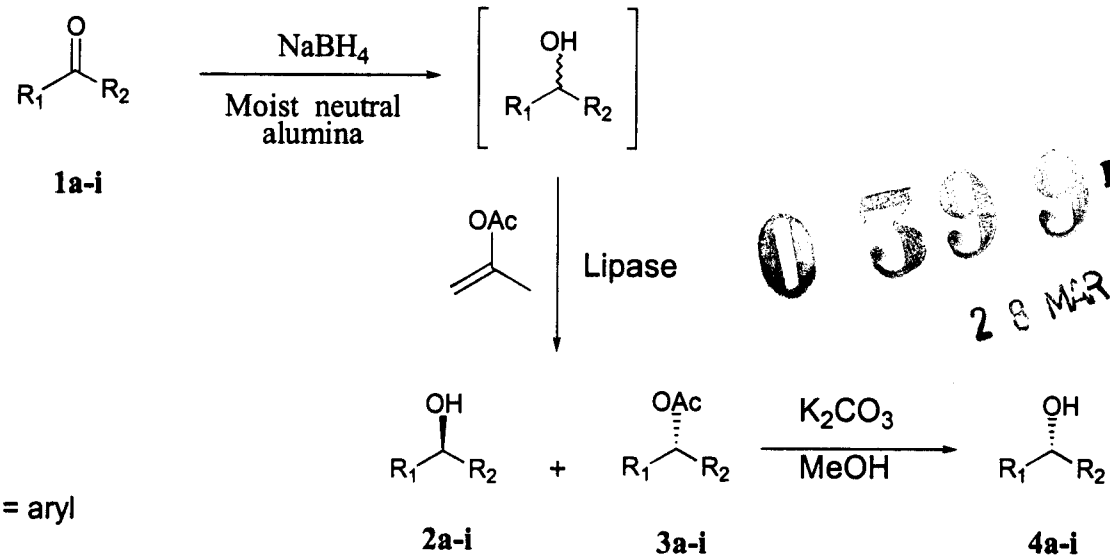
7) A process as claimed in claims 1-6, wherein the enantiomeric excess is >99%.

8) A process as claimed in claim 1-5 wherein the neutral alumina and lipase used are recyclable for one-pot transesterification.

9) An one-pot chemoenzymatic process for the stereoselective preparation of secondary alcohols from corresponding ketones, substantially as herein described with reference to the examples and drawing accompanying this specification.

Dated this .... of..... MARCH 1, ...2002

(SCIENTIST)
Intellectual Property Management Division
Council of Scientific and Industrial Research



1a-i

2a-i

3a-i

4a-i

R1 = aryl

R2 = alkyl

Figure 1

APPLICANTS
CSIR

Secondary alcohols having enantiomeric purity are important synthetic intermediates and are useful chiral auxiliaries in both synthetic and analytical chemistry applications *(J. Chem. Soc., Chem. Commun.* **1988,** 1459). Because of the wide applicability of secondary alcohols; there has been an interest and demand to synthesize them in enantiomerically pure form. Many methods have been reported in the literature based on enantioselective reduction of the corresponding ketones. *(Tetrahedron. Lett.* **2000,** *41,* 4135; *Tetrahedron: Asymmetry* **2000,** *11,* 3671). These include the use of chiral reducing agents, chiral boranes, chiral catalysts, enantioselective homogeneous hydrogenation, and the reduction employing the whole cells.

On the other hand these chiral secondary alcohols have been synthesized by enzymatic transesterification of the racemic alcohols or by enzymatic hydrolysis of the corresponding esters. *(Tetrahedron Lett.* **2001,** *42* 1107). The recent studies on the use of enzymes in low polarity organic solvents initially discovered by Klibanov, has allowed to extend these reactions for the enzymatic resolution by esterification and transesterification *(Proc. Natl. Acad. Sci.* USA **1985**, *82,* 3192). The resolution based on enzymatic transesterification overcomes some of the important practical problems associated with the enzymatic hydrolysis such as, low solubility of many organic compounds in water, the recovery of the enzyme for recycling and the need for pH adjustment during the reaction process. A recent study on the alumina-assisted reduction of carbonyl compounds with sodium borohydride in an aprotic solvent like hexane *(Can. J. Chem.* **1998,** *76,* 1916), and our interest in biotransformations prompted us to explore the transesterification employing the lipase in the same pot for the enantioselective preparation of secondary alcohols.

The main objective of the present invention is to provide a one-pot chemoenzymatic process for the stereoselective preparation of secondary alcohols from corresponding ketones.

In the drawings accompanying this specification Figure-1 is the schematic representation of this process towards the preparation of both enantiomers of secondary alcohols in high enantiomeric excess.

Accordingly, the present invention provides a one-pot chemoenzymatic process for the stereo selective preparation of chiral secondary alcohols from corresponding ketones which comprises:

a) reacting ketone selected from the group consisting of acetophenone, propiophenone, 2-chloropropiophenone, 4-benzyloxy acetophenone, 4-allyloxy acetophenone,4-allyloxy acetophenone and 4-nitro acetophenone with a reducing agent sodium borohydride in a molar ratio in the range of 1:1.5-1:2.5 in an organic solvent as herein described at a temperature in the range of 30-50^{0}C for a period of 2-4 hrs,
b) adding Lipase selected from the group consisting of *Pseudomonas cepacia* lipase (Amano PS), immobilized lipase PS-amano C, PS-Amano D, and *Pseudomonas fluorescence* and an acetylating agent selected from isopropenyl acetate and vinyl acetate to the above said reaction mixture,
c) stirring the above said reaction mixture for a period of 4-12 hrs, at a temperature of 20-30^{0}C to obtain the corresponding recimic alcohol (2) and recemic acetate (3),
d) reacting the above said recemic acetate (3) with potassium bicarbonate in an organic solvent as mentioned in step a), at a temperature of 20-30^{0}C for period of 2-4 hrs to obtain the desired recemic alcohol (4)

In yet another embodiment the organic solvent used is selected from the group consisting of hexane, diisopropyl ether, t-butylmethyl ether, tetrahydrofuran and toluene.

In yet another embodiment the lipase used is selected from the group consisting of Pseudomonas cepacia lipase (Amano PS), immobilized lipase PS-Amano C, PS-Amano D, and Pseudomonas fluorescence.

In yet another embodiment the acetylating agent used is selected from vinyl acetate and isopropenyl acetate.

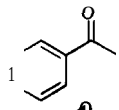
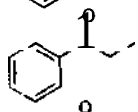
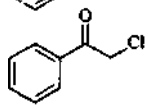
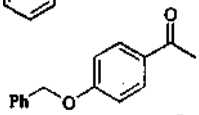
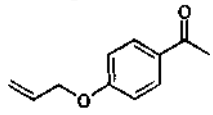
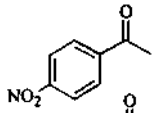
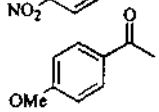
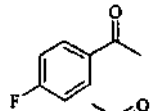
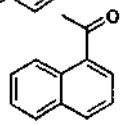
In yet another embodiment the enantiomeric excess is >99%.

In yet another embodiment the neutral alumina and lipase used are recyclable for one-pot transesterification.

An enzymatic process for the stereoselective preparation of secondary alcohols from the corresponding carbonyl compounds, which comprises reduction of ketones with sodium borohydride and moist neutral alumina in hexane. The reduction products thus obtained were further subjected for lipase-mediated transesterification process in the same pot (Table 1).

In yet another embodiment of the present invention the alcohol and the ester formed in the kinetic resolution were separated by column chromatography. Absolute configuration was ascertained by the values of optical rotation and the enantiomeric purity was confirmed by HPLC employing chiral column.

Table 1. Lipase[a] mediated resolution of secondary alcohols in one-pot reduction of their corresponding carbonyl compounds.

Entry	Substrate (1)	Time (h)[b]	2			3		
			Yield (%)[c]	E.e. (%)[d]	Configuration[e]	Yield (%)[c]	E.e. (%)[d]	Configuration[e]
a		4	50	>99	5	48	>99	*R*
			43	>99	*S*	49	>99	
		10	48	>99		44	>99	
			40	>99		42	98	
			38	>99		45	>99	
			45	>99		49	>99	
		8	46	—		44	98	
		10	41			43		
		12	38	70		42	>99	

*Lipase PS-C, (0.5 equiv w/w), isopropenyl acetate, (6 equiv), rt.

[b] Time taken for transesterification.

[c] Isolated yields after column chromatography.

[d] Determined by chiral HPLC.

[e] The absolute configuration assigned by sign of rotation.

[f] Not determined.

The process of the present invention is illustrated below:

1. Use of sodium borohydride in presence of moist neutral alumina for reduction of ketones.
2. Reduction of ketones was carried out at 40 °C for 3-5 hours.
3. After the complete reduction, the racemic alcohol thus obtained was subjected for lipase-mediated transesterification in the same pot.
4. Lipase-mediated transesterification of racemic alcohols were carried out at room temperature for 4-24 hours.
5. Filtration followed by concentration of filtrate leaves the oily residue, which was purified by column chromatography to separate the enantiopure alcohol and acetate.
6. Various solvents like hexane, diisopropyl ether, t-butylmethyl ether, tetrahydrofuran, and toluene were employed.
7. Acetylating agents such as vinyl acetate and isopropenyl acetate were used for acetylation.
7. Different lipases like *Pseudomonas cepacia* lipase (Amano PS), immobilized lipase PS-Amano C, PS-Amano D, *Pseudomonas fluorescence* were screened for the enzymatic resolution.
9. Different substituted acetophenones were studied for this one-pot reaction process.
10. The neutral alumina and lipase used were recycled for one-pot transesterification.
11. Absolute configuration of chiral alcohol and acetate were ascertained by the value of optical rotation.
12. The enantiomeric excess was determined by HPLC employing chiral columns.

The following examples are given by way of illustration and they should not be construed to limit the scope of the present invention.

Example 1

1-Phenyl-(1S)-ethane-1-ol(2a): To a solution of acetophenone (1 mmol) in 10 mL of hexane was added previously prepared moist neutral alumina (10 % water; 1.0 g) and $NaBH_4$ (2 mmol). The resulting reaction mixture was stirred at 40 °C for 3 h and monitored for the completion of the reduction by TLC. At the end of the reaction was added Lipase 'Amano' PS-C II (0.5 equiv. w/w) and isopropenyl acetate (0.65 mL). The

reaction was stirred at room temperature for 4 h. It was then filtered through celite, diluted with EtOAc and washed with water. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure to give an oily residue, which was purified by silica gel column chromatography to obtain enantiomerically pure acetate 3a and alcohol.2a. Yield = 50%; >99% ee (HPLC analysis was performed by employing Chiracel, OJ-H column, Daicel employing hexane/isopropanol = 90/10 as mobile phase, 0.5 mL/min flow and monitored at 254 nm wavelength); $[\alpha]^{25}_D$ –66.51 *(c* 1.4, $CHCl_3$); IR (KBr) 3444 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): 5 1.5 (3H, d, *J* = 6.89 Hz), 4.8 (1H, q, *J* = 6.89 Hz), 7.2-7.4 (5H, m); EIMS *(m/z):* 122 (M+), 107 (M^+-17).

1-Phenyl-(1R)-ethyl acetate (**3a**): yield = 48%; >99% ee (HPLC analysis was performed by employing Chiracel OD column, Daicel employing hexane/isopropanol = 85/15 (v/v) as mobile phase, 0.7 mL/min flow and monitored at 254 nm wavelength); $[\alpha]^{25}_D$ +86.66 *(c* 1.5, $CHCl_3$); IR (KBr) 1732 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): 6 1.5 (3H, d, *J* = 6.76 Hz), 2.1 (3H, s), 5.9 (1H, q, *J* = 6.76 Hz), 7.2-7.4 (5H, m); EIMS (m/z): 164 (M^+), 122 (M^+-42).

Example 2

1-Phenyl-(1S)-propan-1-ol (**2b**): To a solution of propiophenone (1 mmol) in 10 mL of hexane was added previously prepared moist neutral alumina (10 % water; 1.0 g) and $NaBH_4$ (2 mmol). The resulting reaction mixture was stirred at 40 °C for 3 h and monitored for the completion of the reduction by TLC. At the end of the reaction was added Lipase 'Amano' PS-C II (0.5 equiv. w/w) and isopropenyl acetate (0.65 mL). The reaction was stirred at room temperature for 4 h. It was then filtered through celite, diluted with EtOAc and washed with water. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure to give an oily residue, which was purified by silica gel column chromatography to obtain enantiomerically pure acetate 3b and alcohol 2b. Yield = 43%; >99% ee (HPLC analysis was performed by employing Chiracel, OJ-H column, Daicel employing hexane/isopropanol = 95/5 as mobile phase, 0.5 mL/min flow and monitored at 254 nm wavelength); $[\alpha]^{25}_D$ –45.60 *(c* 1.3, $CHCl_3$); IR (KBr) 3369 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 8 0.9 (3H, t, *J* = 9.2 Hz), 1.7-1.9 (2H, m), 4.6 (1H, t, *J* = 6.88 Hz), 7.2-7.4 (5H, m); EIMS *(m/z):* 136 (M^+).

1-Phenyl-(1R)-propyl acetate (**3b**): Yield = 49%; >99% ee (HPLC analysis was performed by employing Chiracel, OJ-H column, Daicel employing hexane/isopropanol

= 95/5 as mobile phase, 0.5 mL/min flow and monitored at 254 nm wavelength); $[\alpha]^{25}_D$ +104.68 (c 1.7, $CHCl_3$); IR (KBr) 1737 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 5 0.9 (3H, t, *J* = 4.28 Hz), 1.7-1.9 (2H, m), 2.1 (3H, s), 5.6 (1H, t, *J* = 3.21 Hz), 7.2-7.4 (5H, m); EIMS (*m/z*): 178 (M^+), 136 (M^+ - 42).

Example 3

2-Chloro-1-phenyl-(1R)-ethan-1-ol (**2c**): To a solution of 2-chloropropiophenone (1 mmol) in 10 mL of hexane was added previously prepared moist neutral alumina (10 % water; 1.0 g) and NaBH4 (2 mmol). The resulting reaction mixture was stirred at 40 °C for 3 h and monitored for the completion of the reduction by TLC. At the end of the reaction was added Lipase 'Amano' PS-C II (0.5 equiv. w/w) and isopropenyl acetate (0.65 mL). The reaction was stirred at room temperature for 10 h. It was then filtered through celite, diluted with EtOAc and washed with water. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure to give an oily residue, which was purified by silica gel column chromatography to obtain enantiomerically pure acetate 3c and alcohol 2c. Yield = 48%; >99% ee (HPLC analysis was performed by employing Chiracel OD column, Daicel employing hexane/isopropanol = 85/15 (v/v) as mobile phase, 0.7 mL/min flow and monitored at 254 nm wavelength); $[\alpha]^{25}_D$ -56.20 (c 1.1, $CHCl_3$); IR (KBr) 3499 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 5 2.6 (1H, d, *J* = 6.89 Hz), 3.5-3.9 (2H, m), 5.9 (1H, m), 7.3-7.5 (5H, m).

2-Chloro-1-phenyl-(1S)-ethylacetate (3c): Yield = 44%; >99% ee (HPLC analysis was performed by employing Chiracel OD column, Daicel employing hexane/isopropanol = 85/15 (v/v) as mobile phase, 0.7 mL/min flow and monitored at 254 nm wavelength); $[\alpha]^{25}_D$ +76.60 (c 1.1, $CHCl_3$). IR (KBr); 1747 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 6 2.2 (3H, s), 3.7-3.9 (2H, m), 5.9 (1H, m), 7.3-7.4 (5H, m); EIMS *(m/z):* 162 (M^+-36), 120 (M^+-78).

Example 4

1-(4-Benzyloxyphenyl)-(1S)-ethan-1-o(**2d**): To a solution of 4-benzyloxy acetophenone (1 mmol) in 10 mL of hexane was added previously prepared moist neutral alumina (10 % water; 1.0 g) and NaBH4 (2 mmol). The resulting reaction mixture was stirred at 40 °C for 3 h and monitored for the completion of the reduction by TLC. At the end of the reaction was added Lipase 'Amano' PS-C II (0.5 equiv. w/w) and isopropenyl acetate (0.65 mL). The reaction was stirred at room temperature for 4 h. It was then filtered

through celite, diluted with EtOAc and washed with water. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure to give an oily residue, which was purified by silica gel column chromatography to obtain enantiomerically pure acetate 3d and alcohol 2d. Yield = 40%; mp 64-65 °C; >99% ec (HPLC analysis was performed by employing Chiracel OD column, Daicel employing hexane/isopropanol = 85/15 (v/v) as mobile phase, 0.7 mL/min flow and monitored at 254 nm wavelength); $[\alpha]^{25}_{D}$ -31.80 (*c* 1.2, $CHCl_3$); IR (KBr) 3373 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 8 1.5 (3H, d, *J* = 6.89Hz), 4.8 (1H, q, *J* =6.89 Hz), 5.1 (2H, s), 6.9 (2H, d, *J* = 9.19Hz), 7.2-7.5 (6H, m); EIMS (*m/z*):228 (M^+).

*1-(4-Benzyloxyphenyl)-(1R)-ethyl*acetate (3d): Yield = 42%; mp 50-51 °C; 98% ee (HPLC analysis was performed by employing Chiracel OD column, Daicel employing hexane/isopropanol = 85/15 (v/v) as mobile phase, 0.7 mL/min flow and monitored at 254 nm wavelength); $[\alpha]^{25}_{D}$ +89.80 (*c* 1.4, $CHCl_3$); IR (KBr) 1732 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): 8 1.5 (3H, d, *J* = 6.89 Hz), 2.1 (3H, s), 5.1 (1H, *q*,*J*= 6.89 Hz), 5.1 (2H, s) 6.9 (2H d, *J* = 9.19 Hz), 7.3 (2H, a, *J* = 9.19 Hz) 7.4-7.5 (5H, m); EIMS (m/z): 270

Example 5

1-(4-Allyloxyphenyl)-(1S)-ethan-1-o(2e): To a solution of 4-allyloxy acetophenone (1 mmol) in 10 mL of hexane was added previously prepared moist neutral alumina (10 % water; 1.0 g) and NaBH4 (2 mmol). The resulting reaction mixture was stirred at 40 °C for 3 h and monitored for the completion of the reduction by TLC. At the end of the reaction was added Lipase 'Amano' PS-C II (0.5 equiv. w/w) and isopropenyl acetate (0.65 mL). The reaction was stirred at room temperature for 6 h. It was then filtered through celite, diluted with EtOAc and washed with water. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure to give an oily residue, which was purified by silica gel column chromatography to obtain enantiomerically pure acetate 3e and alcohol 2e. Yield = 38%; >99% ee (HPLC analysis was performed by employing Chiracel, OJ-H column, Daicel employing hexane/isopropanol = 95/5 as mobile phase, 0.5 mL/min flow and monitored at 254 nm wavelength); $[\alpha]^{25}_{D}$ -35.40 (*c* 0.7, $CHCl_3$); IR (KBr) 3417 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): 8 1.4 (3H, d, *J* = 5.71 Hz), 4.5 (3H, d, *J* = 5.71Hz), 4.8 (1H, *q*,*J*= 5.72 Hz), 5.2

(1H, dd, J= 2.85, 11.42 Hz), 5.4 (1H, d, J = 17.14 Hz), 6.0 (1H, m), 6.8 (2H, d, J = 8.57 Hz) 7.2 (2H, d, J = 8.57); EIMS *(m/z):* 178 (M^+), 163 (M^+-15).

1-(4-Allyloxyphenyl)-(1R)-ethyl acetate (**3e**): Yield = 45%; >99% ee (HPLC analysis was performed by employing Chiracel, OJ-H column, Daicel employing hexane/isopropanol = 90/10 as mobile phase, 0.5 mL/min flow and monitored at 254 nm wavelength); $[\alpha]^{25}_D$ +116.50 *(c* 1.2, $CHCl_3$); IR (KBr) 1734 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): *d* 1.5 (3H, d, J= 6.89 Hz), 2.0 (3H, s), 4.5 (2H, m, J = 5.74 Hz), 5.3 (1H, d, J = 10.34 Hz), 5.4 (1H, d, J = 17.47 Hz), 5.7-5.9 (1H, q, J = 6.89 Hz), 5.9-6.2 (1H, m) , 6.8 (2H, d, J = 8.27 Hz) 7.3 (2H, d, J = 8.27); EIMS *(m/z):* 220 (M^+).

Example 6

1-(4-Nitrophenyl)-(1S)-ethan-1-o(**2f**): To a solution of 4-nitro acetophenone (1 mmol) in 10 mL of hexane was added previously prepared moist neutral alumina (10 % water; 1.0 g) and NaBH4 (2 mmol). The resulting reaction mixture was stirred at 40 °C for 3 h and monitored for the completion of the reduction by TLC. At the end of the reaction was added Lipase 'Amano' PS-C II (0.5 equiv. w/w) and isopropenyl acetate (0.65 mL). The reaction was stirred at room temperature for 6 h. It was then filtered through celite, diluted with EtOAc and washed with water. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure to give an oily residue, which was purified by silica gel column chromatography to obtain enantiomerically pure acetate 3f and alcohol 2f. Yield = 45%; >99% ee (HPLC analysis was performed by employing Chiracel, OJ-H column, Daicel employing hexane/isopropanol = 95/5 as mobile phase, 0.5 mL/min flow and monitored at 254 nm wavelength); $[\alpha]^{25}_D$ -32.72 *(c* 1.0, $CHCl_3$); IR (KBr) 3411 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): 8 1.5 (3H, d, 7= 7.56 Hz), 5.9 (1H, q, J =7.56 Hz), 7.5 (2H, d, J= 8.10Hz), 8.2 (2H, d, J = 8.10 Hz).

1-(4-Nitrophenyl)-(1R)-ethyl acetate (**3f**): Yield = 49%; >99% ee (HPLC analysis was performed by employing Chiracel, OJ-H column, Daicel employing hexane/isopropanol = 95/5 as mobile phase, 0.5 mL/min flow and monitored at 254 nm wavelength); $[\alpha]^{25}_D$ +99.20 *(c* 1.4, $CHCl_3$); IR (KBr) 1734 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): 6 1.5 (3H, d, J = 7.59 Hz), 2.0 (3H, s), 5.9 (1H, q, J = 7.59 Hz), 7.5 (2H, d, J= 8.86) 8.2 (2H, d, J = 8.86 Hz); EIMS *(m/z):* 167 (M^+-42).

Example 7

1-(4-Methoxyphenyl)-(1S)-ethan-1-ol (2g): To a solution of 4-methoxy acetophenone (1 mmol) in 10 mL of hexane was added previously prepared moist neutral alumina (10 % water; 1.0 g) and $NaBH_4$ (2 mmol). The resulting reaction mixture was stirred at 40 °C for 3 h and monitored for the completion of the reduction by TLC. At the end of the reaction was added Lipase 'Amano' PS-C II (0.5 equiv. w/w) and isopropenyl acetate (0.65 mL). The reaction was stirred at room temperature for 8 h. It was then filtered through celite, diluted with EtOAc and washed with water. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure to give an oily residue, which was purified by silica gel column chromatography to obtain enantiomerically pure acetate 3g and alcohol 2g. Yield = 46%; >99% ee (HPLC analysis was performed by employing Chiracel OD column, Daicel employing hexane/isopropanol = 85/15 (v/v) as mobile phase, 0.7 mL/min flow and monitored at 254 nm wavelength); $[\alpha]^{25}_D$ -59.00 (*c* 1.0, $CHCl_3$); IR (KBr) 3523 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): 5 1.5 (3H, d, J = 6.86 Hz), 1.8 (3H, s), 4.8 (1H, q, J = 6.86 Hz), 6.8 (2H, d, J = 9.15), 7.3 (2H, d, J = 9.15Hz); FABMS: 152 (M^+).

1-(4-Methoxyphenyl)-(1R)-ethyl acetate (3g): Yield = 44%; 98% ee (HPLC analysis was performed by employing Chiracel OD column, Daicel employing hexane/isopropanol = 85/15 (v/v) as mobile phase, 0.7 mL/min flow and monitored at 254 nm wavelength); $[\alpha]^{25}_D$ +134 (c 1.4, $CHCl_3$); IR (KBr) 1739 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): 8 1.6 (3H, d, J = 7.64 Hz), 2.1 (3H, s), 3.8 (3H, s), 5.8 (1H, q, J = 7.64 Hz), 6.8 (2H, d, J = 8.91 Hz) 7.2-7.4 (2H, d, J = 8.91 Hz); EIMS (*m/z*): 194 (M^+).

Example 8

1-(4-Fluorophenyl)-(1S)-ethan-1-ol (2h): To a solution of 4-fluoro acetophenone (1 mmol) in 10 mL of hexane was added previously prepared moist neutral alumina (10 % water; 1.0 g) and NaBH4 (2 mmol). The resulting reaction mixture was stirred at 40 °C for 3 h and monitored for the completion of the reduction by TLC. At the end of the reaction was added Lipase 'Amano' PS-C II (0.5 equiv. w/w) and isopropenyl acetate (0.65 mL). The reaction was stirred at room temperature for 10 h. It was then filtered through celite, diluted with EtOAc and washed with water. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure to give an oily residue, which was purified by silica gel column chromatography to obtain

enantiomerically pure acetate 3h and alcohol 2h. Yield = 41%; $[\alpha]^{25}_D$ -35.60 (*c* 0.5, $CHCl_3$); IR (KBr) 3457 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): 5 1.4 (3H, d, *J* = 6.89 Hz), 1.9 (1H, s), 4.8 (1H, q, *J* = 6.89 Hz), 7.0 (2H, t, *J* = 8.04 Hz), 7.2-7.4 (2H, dd, *J* = 8.04, 2.29 Hz); EIMS (*m/z*): 140 (M^+), 125 (M^+-15).

1-(4-fluorophenyl)-(1R)-ethylacetate (**3h**): Yield = 43%; $[\alpha]^{25}_D$ -94.20 (c 1.1, $CHCl_3$); IR (KBr) 1732 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): 8 1.5 (3H, d, *J* = 6.41 Hz), 2.0 (3H, s), 5.8 (1H, q, *J* = 6.41 Hz), 7.0 (2H, t, *J*= 8.97 Hz), 7.2-7.4 (2H, dd, *J*= 8.97, 2.56 Hz).

Example 9

1-(1-Napthyl)-(1S)-ethan-1-ol (**2i**): To a solution of 4-fluoro 1-acetonaphthone (1 mmol) in 10 mL of hexane was added previously prepared moist neutral alumina (10 % water; 1.0 g) and $NaBH_4$ (2 mmol). The resulting reaction mixture was stirred at 40 °C for 3 h and monitored for the completion of the reduction by TLC. At the end of the reaction was added Lipase 'Amano' PS-C II (0.5 equiv. w/w) and isopropenyl acetate (0.65 mL). The reaction was stirred at room temperature for 12 h. It was then filtered through celite, diluted with EtOAc and washed with water. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure to give an oily residue, which was purified by silica gel column chromatography to obtain enantiomerically pure acetate 3i and alcohol 2i. Yield = 38%; 70% ee (HPLC analysis was performed by employing Chiracel OD column, Daicel employing hexane/isopropanol = 85/15 (v/v) as mobile phase, 0.7 mL/min flow and monitored at 254 nm wavelength); $[\alpha]^{25}_D$ –44.60 (*c* 1.4, $CHCl_3$); IR (KBr) 3369 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): *d* 1.7 (3H, d, *J* = 7.36 Hz), 5.7 (1H, q, *J* = 7.36 Hz), 7.5 (3H, m), 7.7 (1H, d, *J* = 7.89 Hz) 7.9 (1H, d, *J*= 7.89 Hz), 8.2 (1H, d, *J* = 7.89 Hz); EIMS *(m/z):* 172 (M^+), 157 (M^+-15).

1-(1-Napthyl)-(1R)-ethylacetate (**3i**): Yield = 42%; >99% ee (HPLC analysis was performed by employing Chiracel OD column, Daicel employing hexane/isopropanol = 85/15 (v/v) as mobile phase, 0.7 mL/min flow and monitored at 254 nm wavelength); $[\alpha]^{25}_D$ +52.70 (c 1.1, $CHCl_3$); IR (KBr) 1739 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): 8 1.7 (3H, d, *J* = 7.22 Hz), 2.1 (3H, s), 6.6 (1H, q, *J* = 7.22 Hz), 7.4-7.6 (5H, m), 7.2-7.9 (2H, m), 8.1 (1H, d, *J* = 7.3Hz); EIMS (m/z): 214 (M^+), 172 (M^+-42).

General procedure for hydrolysis of acetate to alcohol (A): To a solution of acetate 3 (3 mmol) in 30 mL of methanol was added K_2CO_3 (10 mmol) and stirred at room

temperature for 6 hrs. After complete hydrolysis of ester as indicated by TLC, the reaction mixture was subjected to filtration. The residue is treated with ethyl acetate (2x15ml). The organic layers were combined and solvents were evaporated to get the corresponding alcohol in almost quantitative yields (98%).

Racemic alcohol (2a-i):

The racemic alcohols were prepared by sodium borohydride reduction of the ketone in methanol, as an authentic sample for comparison on HPLC.

Racemic acetate (3a-i):

The racemic acetates were prepared by treating the racemic alcohol with acetic anhydride in presence of triethyl amine and catalytic amount of DMAP, as an authentic sample for comparison on HPLC.

The main advantages of the present invention ?re:

Reduction reaction leading to chirally pure intermediates is most frequently used transformation in organic synthesis. Enantiopure secondary alcohols are important chiral auxiliaries in organic synthesis. These types of chiral secondary alcohols are found in many naturally occurring biologically active compounds. In recent years there has been demand for the chiral secondary alcohols, which are found in number of biologically active intermediates.

Optically pure secondary alcohols have been obtained in good yields and high enantiomeric excess by one-pot reduction of ketones followed by lipase-mediated transesterification. The faster reaction rates with high selectivity in organic media like hexane and environmentally acceptable reaction conditions provides a practical *in situ* biocatalytic resolution process of the secondary alcohols from their carbonyl precursors under mild conditions.