Pergamon

Tetrahedron: *Asymmetry* 12 (2001) 2457–2462

TETRAHEDRON: *ASYMMETRY*

Humicola lanuginosa lipase-catalyzed enantioselective resolution of β-hydroxy sulfides: versatile synthons for enantiopure β-hydroxy sulfoxides

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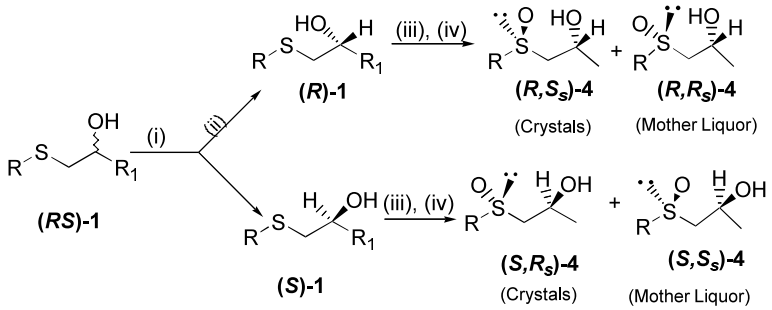
Received 4 September 2001; accepted 1 October 2001

Abstract—*Humicola lanuginosa* lipase-catalyzed acylation of β-hydroxy sulfides provides both the (*R*)- and (*S*)-enantiomers in high enantiomeric purity. In two cases the resolved hydroxy sulfides were oxidized to give β-hydroxy sulfoxides in >99% e.e. The effect of substituents on enantioselectivity is discussed. © 2001 Elsevier Science Ltd. All rights reserved.

1. Introduction

Enantiopure functionalized secondary alcohols are important synthetic intermediates and useful chiral auxiliaries both for analytical and synthetic applications.[1] The presence of a sulfur atom placed at an appropriate position from the hydroxy group provides unique synthetic versatility.[2] Thus, enantiopure hydroxy sulfides serve as intermediates in the synthesis of naturally occurring spiroketal pheromones,[3] chiral oxiranes,[4] thiiranes,[5] tetrahydrofurans,[6] and 4-acetoxyazetidinone.[7] The available synthetic approaches for obtaining enantiopure hydroxy sulfides involve stereoselective reduction of phenylthio ketones using baker's yeast[3,8] or asymmetric chiral ruthenium complexes[9] and are plagued with either the availability of only one enantiomer or moderate enantioselectivity. The lipase-catalyzed resolution of hydroxy sulfides or their esters provides an alternative approach[10] and have found that *Humicola lanuginosa* lipase (HLL), a cheap detergent lipase, rarely used for resolution of organic molecules resolves β-hydroxy sulfides to give both the (*R*)- and (*S*)-enantiomers of **1a**–**1g** in high enantiomeric purity.

Furthermore, oxidation of the enzymatically-resolved enantiomers **1a**–**1b** with *m*-CPBA, followed by fractional crystallization provides a convenient route to the enantiopure β-hydroxy sulfoxides (Scheme 1), which find widespread application as chiral intermediates[11] and chiral catalysts.[12] Generally, β-hydroxy sulfoxides are synthesized by the stereoselective reduction[13,14] of chiral β-ketosulfoxides, which are obtained through an approach requiring several steps, starting with Andersen's resolution.[15] This method, in addition to



Scheme 1. (i) Lipase/VA; (ii) base; (iii) *m*-CPBA; (iv) fractional crystallization.

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PII: S0957-4166(01)00434-7

Table 1. Enantioselective acylation of alcohols (*R*,*S*)-**1** and (*R*,*S*)-**3** with HLL[a]

Entry	Substrate	Time[b] (h)	Conv. (%)[c]	Yield[d] of (*S*)-alc.	E.e.[e] (*S*)-alc.	Yield[d,f] of (*R*)-alc.	E.e.[e] (*R*)-alc.	E_s[g]
1	**1a**	12.5	46	49	81	45	99	500
2	**1b**	11	46	50	76	44	92	62
3	**1c**	11	37	51	41	36	95	61
4	**1d**	12	48	51	78	46	88	37
5	**1e**	7	33	56	40	30	88	23
6	**1f**	12	43	52	66	43	90	38
7	**1g**	28	42	53	70	39	88	124
8	**3**	8	44	52	62	42	84	23

[a] The substrate:enzyme ratio is 1:2 w/w.
[b] Reaction performed with HLL preincubated at 39±1°C for 72 h.
[c] Percentage conversion was calculated with the help of ^{1}H NMR.
[d] Yields refer to pure isolated products after column chromatography.
[e] E.e. calculated by ^{1}H NMR analysis of the corresponding acetylmandelic acid ester of the alcohol.
[f] Overall yield of alcohol derived from hydrolysis of the initially formed chiral acetate.
[g] Enantiomeric ratio (*E*) values were determined from the e.e. of residual substrate and extent of conversion. (Chen, Ch-Sh; Fujimoto, Y.; Girdaukas, G.; Sih, J. C. *J. Am. Chem. Soc.* **1982**, *104*, 7294).

being inconvenient provides only the (*R*)-configured sulfinyl compound. Herein, we report the first-time synthesis of enantiomerically pure (R,S_s)- and (S,R_s)-β-hydroxy sulfoxides without using an optically active starting material through lipase-catalyzed kinetic resolution.

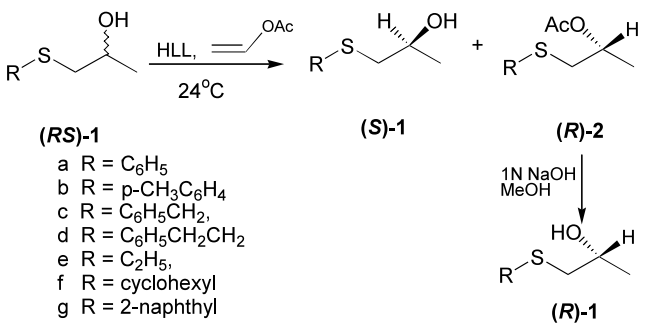
2. Results and discussion

Optimization of the conditions for the resolution of β-hydroxy sulfide **1a** with different lipases showed HLL to be a better catalyst.[16] A typical procedure involves stirring a solution of **1a** (840 mg, 5 mmol) and HLL (1.68 g, 2 equiv. w/w) with vinyl acetate (4.5 mL, 10 equiv.) used both as reagent and solvent, at 25±1°C. The reaction was monitored by recording ^{1}H NMR spectra of aliquots of the reaction mixture taken at regular intervals. The reaction was stopped at 46% conversion (12.5 h) by filtration of the enzyme and (*R*)-**2a** and (*S*)-**1a** were separated by column chromatography. (*R*)-**2a** was hydrolyzed with 1N methanolic NaOH to give (*R*)-**1a**. The e.e. of (*R*)-**1a** was found to be 99% and (*S*)-**1a** had e.e. of 81% (Table 1).[17] This reaction has enantiomeric ratio (*E* value) of 500.

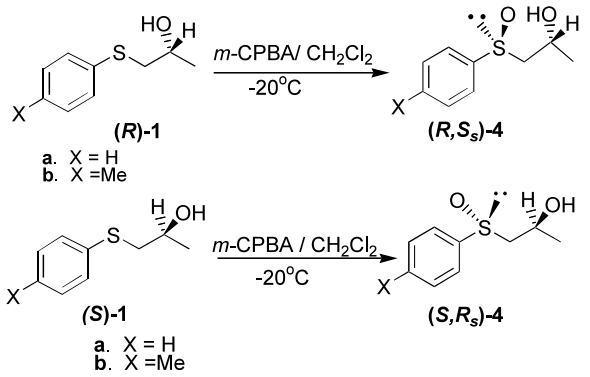
All other β-hydroxy sulfides **1b**–**1g** were then resolved under similar conditions (Scheme 2). It was observed that aryl sulfide derivatives (entries 1 and 2) show better enantioselectivity than alkyl derivatives (entries 5 and 6). Also, in the case of aryl group-containing substrates (entries 1, 3, and 4), the placement of the phenyl ring away from the sulfur atom decreases the *E* progressively from 500 (entry 1) to 61 (entry 3) to 37 (entry 4). Clearly, increasing spacer length between the phenyl ring and the sulfur atom decreases the enantioselectivity.

To investigate the role of the sulfur atom in enantioselective recognition of the (*R*)-enantiomer by HLL, resolution of (±)-1-phenoxypropan-2-ol **3** was carried out to obtain (*R*)-**3** (84% e.e.) and (*S*)-**3** in 62% e.e. ($E=23$). The replacement of the sulfide with an ether linkage lowers the enantioselectivity. Thus, both of these observations show that the phenylthio group present β- to the hydroxy group increases the enantiopreference of HLL in favor of the (*R*)-enantiomer. Therefore, *Humicola lanuginosa* lipase (HLL) catalyzes the acylation of 1-alkyl/aryl-thiopropan-2-ols in vinyl acetate to provide the (*S*)-enantiomers (40–81% e.e.) and the (*R*)-enantiomers (88–99% e.e.) with *E* values ranging from 23 to 500.

On stirring (*R*)-**1b** with *m*-CPBA in dichloromethane (Scheme 3) at −20°C afforded a mixture of the



Scheme 2.



Scheme 3.

Table 2. Synthesis of β-hydroxy sulfoxides by *m*-CPBA oxidation oxidation

β-Hydroxy sulfide	β-Hydroxy sulfoxide				
	Yield (%)	Mp (°C)	$[\alpha]_D^{27}$	% E.e.	Config.
(*R*)-**1a**[a]	40	132–133	−367 (*c* 0.23, CH_2Cl_2)	>99	(R,S_s)
(*S*)-**1a**[a]	40	133–135	+369 (*c* 0.75, CH_2Cl_2)	>99	(S,R_s)
(*R*)-**1b**[b]	38	122–123	−343 (*c* 0.60, CH_2Cl_2)	>99	(R,S_s)
(*S*)-**1b**[b]	39	123–124	+343 (*c* 0.50, CH_2Cl_2)	>99	(S,R_s)

[a] Crystallization was carried at 24±1°C (CH_2Cl_2/hexane).
[b] Crystallization was carried at 0–5°C (CH_2Cl_2/hexane).

diastereomeric hydroxy sulfoxides i.e. (R,S_s)-**4b** and (R,R_s)-**4b**. Fractional crystallization of the crude mixture at 0–5°C provided a white crystalline solid (38%, >99% e.e., mp 122–123°C) having $[\alpha]_D^{27} = -343$ (*c* 0.60, CH_2Cl_2). The mother liquor afforded a colorless liquid (62% d.e.), which on comparison of its ^{1}H NMR reported in literature[18] was assigned configuration (R,R_s)-**4b**. So, the crystalline diastereomer was assigned the configuration (R,S_s)-**4b** on the basis of its spectroscopic data. A clear distinction between the two diastereomers could be made from the ^{1}H NMR spectra, the methyl and methine protons in (R,S_s)-**4b** resonates at δ 1.23 and δ 4.31–4.38 ppm, and in case of (R,R_s)-**4b** at δ 1.30 and δ 4.38–4.48 ppm. Similar oxidation of enantiomer (*S*)-**1b** followed by crystallization afforded (S,R_s)-**4b** (39%, >99% e.e., mp: 123–124°C) having $[\alpha]_D^{27} = +343$ (*c* 0.50, CH_2Cl_2). Further, sulfoxidation of (*R*)-**1a** and (*S*)-**1a** with *m*-CPBA provided diastereomeric pairs (R,S_s)-**4a**, (R,R_s)-**4a** and (S,R_s)-**4a**, (S,S_s)-**4a**, respectively. The fractional crystallization of respective diastereomeric pairs provided (R,S_s)-**4a** and (S,R_s)-**4a** as pure crystalline solids (Table 2). To the best of our knowledge, (R,S_s)-**4a** and (R,S_s)-**4b** are the first examples of β-hydroxy sulfoxides having (*S*)-configuration at sulfur.

3. Conclusion

Our present studies have demonstrated that *Humicola lanuginosa* lipase (HLL) catalyzed kinetic resolution of racemic β-hydroxy sulfides, coupled with subsequent oxidation with *m*-CPBA provides an effective method for synthesis of enantiopure β-hydroxy sulfoxides which are important chiral intermediates. This method represents a simple alternative to earlier reports,[13,14] as it provides high e.e. under mild reaction conditions without needing any expensive reagents or special expertise. Furthermore, no alternative route to our approach appears to be known for enantiopure sulfoxides (R,S_s)-**4a** and (R,S_s)-**4b**.

4. Experimental

4.1. General

NMR spectra were obtained at 200 (Bruker AC 200E) or 300 MHz for ^{1}H and at 50 or 75 MHz for ^{13}C NMR with Me_4Si (in $CDCl_3$) as internal standard. Chemical shifts are expressed as δ downfield from the TMS and *J* values are in Hz. When necessary, assignments were aided by DEPT-135 and decoupling experiments. IR spectra were obtained with a Nicolet Avatar 320 FTIR. Mass spectra were recorded on GCMS-QP-2000 mass spectrometer by EI method. Optical rotations were measured with a Jasco DIP-360 digital polarimeter.

4.2. Synthesis of the racemic substrates

The starting compounds **1a**–**1g** were prepared by a slight modification of the method given by Crumbie et al.[8a] for the preparation of **1a** and **1c.** To a solution of sodium ethoxide prepared by dissolving metallic sodium (2.53 g, 0.11 mol) in absolute alcohol (50 mL), the respective thiol (0.10 mol) was then added dropwise. The solution was stirred for 10 min at 10°C and finally a solution of chloroacetone (11.1 g, 9.56 mL, 0.12 mol) in absolute alcohol (10 mL) was added over 15 min. Stirring was continued for 2 h then the mixture was filtered to remove precipitated sodium chloride. The filtrate was concentrated under reduced pressure and the resulting viscous oil was diluted with water (10 mL) and extracted with ethyl acetate (3×50 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give crude alkyl/arylthiopropan-2-one, which was reduced with $NaBH_4$ in ethanol. To a stirred solution of the parent ketone (0.1 mol) in ethanol (30 mL), 1.85 g (0.05 mol) of $NaBH_4$ was added in small portions. The mixture was stirred until the reduction was complete (TLC). The reaction mixture was neutralized with dil. HCl, and extracted with ethyl acetate. The organic layer was dried and evaporated to yield the crude product, which was purified by a column chromatography with 60–120 mesh silica gel using hexane–ethyl acetate (90:10) as eluent. The spectroscopic data of **1a** and **1c** agrees well with that reported earlier.[8]

(*RS*)-1-Phenylthiopropan-2-ol 1a: yellow liquid; yield = 79%; IR (film): 3520, 3070, 2970, 2925, 1561, 1030, 690 cm^{-1}; MS (*m*/*z*): 168 (M^+), 135, 124 (100), 123, 109, 91, 77; ^{1}H NMR ($CDCl_3$): δ 1.27 (d, 3H, J = 6.2 Hz, CH_3), 1.98 (bs, 1H, OH), 2.85 (dd, 1H, J = 13.7 and 8.5 Hz, CH_2), 3.11 (dd, 1H, J = 13.7 and 3.7 Hz, CH_2), 3.78–3.90 (m, 1H, CH), 7.17–7.41 (m, 5H, ArH); ^{13}C NMR/DEPT ($CDCl_3$): δ 22.30 (+ve, CH_3), 43.20 (-ve, CH_2), 66.42 (+ve, CH), 127.17 (+ve, C-Ar), 128.22 (+ve, C-Ar), 131.52 (+ve, C-Ar), 131.98 (C-Ar).

(*RS*)-1-(4-Methylphenyl)thiopropan-2-ol 1b: colorless liquid; yield = 82%; IR (film): 3420, 3080, 2972, 1560, 820 cm^{-1}; MS (*m*/*z*): 182 (M+), 137, 136, 123, 91 (100), 77; ^1H NMR ($CDCl_3$): δ 1.24 (d, 3H, J = 6.3 Hz, CH_3), 2.0 (bs, 1H, OH), 2.33 (s, 3H, CH_3), 2.75 (dd, 1H, J = 13.6 and 8.7 Hz, CH_2), 3.03 (dd, 1H, J = 13.6 and 3.6 Hz, CH_2), 3.70–3.85 (m, 1H, CH), 7.08 (d, 2H, J = 8.0 Hz, ArH), 7.28 (d, 2H, J = 8.0 Hz, ArH); ^{13}C NMR/DEPT ($CDCl_3$): δ 20.52 (+ve, CH_3), 21.56 (+ve, CH_3), 43.12 (-ve, CH_2), 65.42 (+ve, CH), 129.26 (+ve, C-Ar), 129.91 (+ve, C-Ar), 131.70 (C-Ar), 135.67 (C-1).

(*RS*)-1-Benzylthiopropan-2-ol 1c: yellow liquid; yield = 80%; IR (film): 3400, 3082, 2992, 1548, 752 cm^{-1}; MS (*m*/*z*): 182 (M^+), 138, 137, 123 (100), 91, 77; ^1H NMR ($CDCl_3$): δ 1.12 (d, 3H, J = 6.2 Hz, CH_3), 2.09 (bs, 1H, OH), 2.26 (dd, 1H, J = 13.7 and 8.8 Hz, CH_2), 2.49 (dd, 1H, J = 13.7 and 3.6 Hz, CH_2), 3.63 (s, 2H, CH_2), 3.66–3.74 (m, 1H, CH), 7.14–7.22 (m, 5H, ArH); ^{13}C NMR/DEPT ($CDCl_3$): δ 22.08 (+ve, CH_3), 36.19 (-ve, CH_2), 40.09 (-ve, CH_2), 65.72 (+ve, CH), 126.84 (+ve, C-Ar), 128.28 (+ve, C-Ar), 128.72 (+ve, C-Ar), 138.00 (C-Ar).

(*RS*)-1-Phenylethylthiopropan-2-ol 1d: pale yellow oil; yield = 77%; IR (film): 3510, 3020, 2980, 1542, 762 cm^{-1}; MS (*m*/*z*): 196 (M+), 181, 151, 137, 119, 105, 91 (100), 77, 58; ^1H NMR ($CDCl_3$): δ 1.24 (d, 3H, J = 6.2 Hz, CH_3), 2.42 (dd, 2H, J = 13.6 and 8.8 Hz, 1H each of $C\underline{H}_2$-CH(OH)-and OH), 2.70 (dd, 1H, J = 13.6 and 3.5 Hz, $C\underline{H}_2$-CH(OH)-), 2.74–2.92 (m, 4H, 2×CH_2), 3.76–3.82 (m, 1H, CH), 7.16–7.28 (m, 5H, ArH); ^{13}C NMR/DEPT ($CDCl_3$): δ 21.56 (+ve, CH_3), 33.3 (-ve, CH_2), 35.75 (-ve, CH_2), 40.75 (-ve, CH_2), 65.46 (+ve, CH), 125.63 (+ve, C-Ar), 127.75 (+ve, C-Ar), 139.66 (C-Ar).

(*RS*)-1-Ethylthiopropan-2-ol 1e: colorless liquid; yield = 71%; IR (film): 3400, 2969, 2927, 2872, 1454, 1125 cm^{-1}; MS (*m*/*z*): 120 (M+), 105, 76, 75, 61: ^1H NMR ($CDCl_3$): δ 1.24 (d, 3H, J = 6.2 Hz, CH_3), 1.27 (t, 3H, J = 7.4 Hz, CH_3), 2.44 (dd, 1H, J = 13.6 and 8.8 Hz, CH_2), 2.54 (q, 3H, J = 7.4 Hz, $C\underline{H}_2$-CH_3 and OH), 2.71 (dd, 1H, J = 13.6 and 3.6 Hz, CH_2), 3.72–3.86 (m, 1H, CH); ^{13}C NMR/DEPT ($CDCl_3$): δ 14.51 (+ve, $C\underline{H}_3CH_2$), 21.74 (+ve, CH_3), 25.85 (-ve, $C\underline{H}_2CH_3$), 40.62 (-ve, CH_2), 65.43 (+ve, CH).

(*RS*)-1-Cyclohexylthiopropan-2-ol 1f: pale yellow liquid; yield = 74%; IR (film): 3420, 2980, 2950, 1345, 1080 cm^{-1}; MS (*m*/*z*): 174 (M+), 130, 129, 115, 83, 69, 55; ^1H NMR ($CDCl_3$): δ 1.25 (d, 3H, J = 6.2 Hz, CH_3), 1.27–2.05 (complex pattern, 12H, cyclohexyl ring and OH), 2.43 (dd, 1H, J = 13.5 and 9.0 Hz, CH_2), 2.65 (m, 1H, SCH), 2.69 (dd, 1H, J = 13.6 and 3.6 Hz, CH_2), 3.81 (m, 1H, CH); ^{13}C NMR/DEPT ($CDCl_3$): δ 21.63 (+ve, CH_3), 25.3 (-ve, CH_2), 25.58 (-ve, CH_2), 33.31 (-ve, CH_2), 33.46 (-ve, CH_2), 38.97 (-ve, CH_2), 43.35 (-ve, CH_2), 65.84 (+ve, CH).

(*RS*)-1-(2-Naphthyl)thiopropan-2-ol 1g: pink solid; yield = 84%; mp 36–38°C ($CHCl_3$/hexane); IR (KBr): 3500, 3080, 2976, 1080, 720 cm^{-1}; MS (*m*/*z*): 218 (M^+), 174, 173, 159, 127, 91, 76; ^1H NMR ($CDCl_3$): δ 1.30 (d, 3H, J = 6.2 Hz, CH_3), 2.80 (bs, 1H, OH), 2.97 (dd, 1H, J = 13.6 and 8.1 Hz, CH_2), 3.19 (dd, 1H, J = 13.6 and 4.0 Hz, CH_2), 3.84–3.97 (m, 1H, CH), 7.17–7.42 (m, 3H, ArH), 7.65–7.92 (m, 4H, ArH); ^{13}C NMR ($CDCl_3$): δ 21.89 (CH_3), 43.11 (CH_2), 65.62 (CH), 125.78 (C-Ar), 126.51 (C-Ar), 126.98 (C-Ar), 127.58 (C-Ar), 127.87 (C-Ar), 128.50 (C-Ar), 131.80 (C-Ar), 132.67 (C-Ar), 133.55 (C-Ar). Found C, 72.12; H, 5.94; $C_{13}H_{14}OS$ requires C, 71.56; H, 6.42%.

4.3. General procedure for resolution

A solution of the (*RS*)-**1** (5 mmol) and vinyl acetate (4.5 mL, 50 mmol) was stirred with HLL (1.68 g, 2 equiv. w/w) at 24±1°C. The reaction was monitored by taking ^1H NMR of aliquots taken at regular intervals. The reaction was stopped by filtering the mixture through a sintered glass funnel. Concentration of the filtrate followed by column chromatography provided (*R*)-**2** and (*S*)-**1**. (*R*)-**2** (2.3 mmol) was hydrolyzed with 1N NaOH (2.3 mL) in 10 mL solution of methanol and water (4:1) to give (*R*)-**1**.

(*R*)-1-Phenylthiopropan-2-yl acetate 2a: yellow oil: $[\alpha]_D^{27} = -0.9$ (*c* 1.12, CH_2Cl_2); IR (film): 3055, 2980, 2930, 1735, 1110, 760 cm^{-1}; MS (*m*/*z*): 210 (M+), 195, 168, 135, 124, 109 (100), 77, 58; ^1H NMR ($CDCl_3$): δ 1.34 (d, 3H, J = 6.3 Hz, CH_3), 1.96 (s, 3H, $COCH_3$), 2.93 (dd, 1H, J = 13.7 and 6.4 Hz, CH_2), 3.15 (dd, 1H, J = 13.7 and 5.9 Hz, CH_2), 5.00 (sextet, 1H, J = 6.3 Hz, CH), 7.12–7.39 (m, 5H, ArH); ^{13}C NMR/DEPT ($CDCl_3$): δ 18.50 (+ve, CH_3), 20.96 (+ve CH_3), 45.22 (−ve, CH_2), 65.52 (+ve, CH), 127.56 (+ve, C-Ar), 128.12 (+ve, C-Ar), 131.68 (+ve, C-Ar), 132.26 (C-Ar), 170.24 (C=O).

(*R*)-1-(4-Methylphenyl)thiopropan-2-yl acetate 2b: yellow liquid: $[\alpha]_D^{27} = -6.6$ (*c* 1.59, CH_2Cl_2); IR (film): 3075, 2976, 1735, 1580, 830 cm^{-1}; MS (*m*/*z*): 224 (M+), 209, 181, 123 (100), 91, 77, 58; ^1H NMR ($CDCl_3$): δ 1.33 (d, 3H, J = 6.3 Hz, CH_3), 1.97 (s, 3H, $COCH_3$), 2.34 (s, 3H, CH_3), 2.87 (dd, 1H, J = 13.7 and 6.5 Hz, CH_2), 3.09 (dd, 1H, J = 13.7 and 6.0 Hz, CH_2), 4.98 (sextet, 1H, J = 6.3 Hz, CH), 7.08 (d, 2H, J = 8.2 Hz, ArH), 7.19 (d, 2H, J = 8.2 Hz, ArH); ^{13}C NMR/DEPT ($CDCl_3$): δ 18.95 (+ve, CH_3), 20.70 (+ve, CH_3), 20.80 (+ve, CH_3), 39.53 (-ve, CH_2), 69.24 (+ve, CH), 129.45 (+ve, C-Ar), 130.0 (+ve, C-Ar), 132.23 (C-Ar), 135.99 (C-Ar), 169.24 (C=O).

(*R*)-1-Benzylthiopropan-2-yl acetate 2c: yellow liquid; $[\alpha]_D^{27} = +17.2$ (*c* 1.59, CH_2Cl_2); IR (film): 3084, 2962, 1745, 1540, 760 cm^{-1}; MS (*m*/*z*): 224 (M^+), 209, 181, 123, 91 (100), 77; ^1H NMR ($CDCl_3$): δ 1.27 (d, 3H, J = 6.2 Hz, CH_3), 2.04 (s, 3H, $COCH_3$), 2.40 (dd, 2H, J = 13.8 and 6.4 Hz, CH_2), 2.55 (dd, 1H, J = 13.8 and 6.3 Hz, CH_2), 3.64 (s, 2H, CH_2), 5.0 (sextet, 1H, J = 6.3 Hz, CH), 7.16–7.34 (m, 5H, ArH); ^{13}C NMR/DEPT ($CDCl_3$): δ 19.19 (+ve, CH_3), 20.96 (+ve, CH_3), 36.23 (-ve, CH_2), 36.32 (-ve, CH_2), 69.11 (+ve, CH), 126.89 (+ve, C-Ar), 128.31 (+ve, C-Ar), 128.87 (+ve, C-Ar), 137.92 (C-Ar), 169.37 (C=O).

(*R*)-1-Phenylethylthiopropan-2-yl acetate 2d: colorless liquid; $[\alpha]_D^{27}=+8.26$ (*c* 2.31, CH_2Cl_2); IR (film): 2974, 1572, 752 cm^{-1}; MS (*m*/*z*): 238 (M+), 223, 195, 119, 105, 91 (100), 77, 58; ^1H NMR ($CDCl_3$): δ 1.30 (d, 3H, $J=6.2$ Hz, CH_3), 2.05 (s, 3H, $COCH_3$), 2.58 (dd, 1H, $J=13.7$ and 6.4 Hz, CH_2-CH(OH)-), 2.73 (dd, 1H, $J=13.8$ and 6.1 Hz, CH_2-CH(OH)-), 2.81–2.94 (m, 4H, 2×CH_2), 5.01 (sextet, 1H, $J=6.2$, CH), 7.19–7.33 (m, 5H, ArH); ^{13}C NMR/DEPT ($CDCl_3$): δ 18.75 (+ve, OAc), 20.83 (+ve, CH_3), 33.69 (-ve, CH_2), 35.93 (-ve, CH_2), 36.99 (-ve, CH_2), 69.54 (+ve, CH), 125.97 (+ve, C-Ar), 128.10 (+ve, C-Ar), 140.00 (C-Ar), 169.87 (C=O).

(*R*)-1-Ethylthio-propan-2-yl acetate 2e: colorless liquid; $[\alpha]_D^{27}=+14.5$ (*c* 1.71 CH_2Cl_2); IR (film): 2980, 2866, 1750, 1410, 1180 cm^{-1}; MS (*m*/*z*): 162 (M+), 147, 119, 60; ^1H NMR ($CDCl_3$): δ 1.28 (t, 3H, $J=7.4$ Hz, CH_3), 1.33 (d, 3H, $J=6.1$ Hz), 2.05 (s, 3H, $COCH_3$), 2.49–2.63 (overlapping q and AB protons, 3H, CH_2CH_3 and CH_2), 2.70 (dd, 1H, $J=13.6$ and 5.8 Hz, CH_2), 4.93–5.02 (m, 1H, CH); ^{13}C NMR/DEPT ($CDCl_3$): δ 15.62 (+ve, CH_3), 20.56 (+ve, CH_3), 22.84 (+ve, CH_3), 24.62 (-ve, CH_2), 42.24 (-ve, CH_2), 64.62 (+ve, CH), 168.54 (C=O).

(*R*)-1-Cyclohexylthiopropan-2-yl acetate 2f: yellow liquid: $[\alpha]_D^{27}=+17.9$ (*c* 0.68, CH_2Cl_2); IR (film): 2984, 2960, 1745, 1420 cm^{-1}; MS (*m*/*z*): 216 (M+), 201, 173, 115 (100), 83; ^1H NMR ($CDCl_3$): δ 1.29 (d, 3H, $J=6.1$ Hz, CH_3), 1.61–1.94 (complex pattern, 11H, cyclohexyl ring), 2.01 (s, 3H, $COCH_3$), 2.54 (dd, 1H, $J=13.4$ and 7.0, CH_2), 2.65 (dd, 1H, $J=13.4$ and 5.8 Hz, CH_2), 4.86–4.95 (m, 1H, CH); ^{13}C NMR/DEPT ($CDCl_3$): δ 20.23 (+ve, CH_3), 21.84 (+ve, CH_3), 24.53 (-ve, CH_2), 25.23 (-ve, CH_2), 33.65 (-ve, CH_2), 34.68 (-ve, CH_2), 39.68 (-ve, CH_2), 44.24 (-ve, CH_2), 66.44 (+ve, CH), 168.66 (C=O).

(*R*)-1-(2-Naphthyl)thiopropan-2-yl acetate 2g: pale yellow liquid; $[\alpha]_D^{27}=-8.8$ (*c* 1.11, CH_2Cl_2); IR (film): 3060, 2974, 1758, 1140, 760 cm^{-1}; MS (*m*/*z*): 260 (M+), 245, 218, 174, 159, 127, 92; ^1H NMR ($CDCl_3$): δ 1.39 (d, 3H, $J=6.3$ Hz, CH_3), 1.99 (s, 3H, $COCH_3$), 3.09 (dd, 1H, $J=13.8$ and 6.3 Hz, CH_2), 3.32 (dd, 1H, $J=13.7$ and 5.9 Hz, CH_2), 5.09–5.19 (m, 1H, CH), 7.45–7.53 (m, 3H, ArH), 7.77–7.88 (m, 4H, ArH); ^{13}C NMR /DEPT ($CDCl_3$): δ 19.59 (+ve, CH_3), 21.48 (+ve, CH_3), 39.27 (-ve, CH_2), 70.07 (+ve, CH), 126.16 (+ve, C-Ar), 126.95 (+ve, C-Ar), 127.52 (+ve, C-Ar), 127.85 (+ve, C-Ar), 128.03 (+ve, C-Ar), 128.85 (+ve, C-Ar), 133.62 (C-Ar), 134.11 (C-Ar), 170.42 (C=O).

4.4. Oxidation with *m*-CPBA

(*R*,*S*$_s$)-1-Phenylsulfinyl-2-propanol 4a: To a stirred solution of (*R*)-**1a** (286 mg, 1.7 mmol) in dichloromethane (10 mL), kept at −20°C was added *m*-CPBA (346 mg, 2.0 mmol) in small portions. The solution was stirred at −20°C, till the TLC showed no starting material (3 h). Sodium carbonate solution was added to the mixture extracted with dichloromethane and dried (anhydrous Na_2SO_4). Evaporation of the solvent gives a mixture of (*R*,*S*$_s$)-**4a** and (*R*,*R*$_s$)-**4a** (280 mg, 91%); mp 95–97°C. Recrystallization from CH_2Cl_2/hexane (0–5°C) afforded (*R*,*S*$_s$)-**4a** (123 mg, 40%) as white solid (ee >99%); mp: 132–133°C (CH_2Cl_2/hexane); $[\alpha]_D^{27}=-367$ (*c* 0.23, CH_2Cl_2); MS (*m*/*z*): 184 (M^+), 182, 166, 139, 125, 78 (100); ^1H NMR ($CDCl_3$, 200 MHz): δ 1.25 (d, 3H, $J=6.3$ Hz, CH_3), 2.64 (dd, 1H, $J=13.4$ and 1.9 Hz, CH_2), 3.00 (dd, 1H, $J=13.4$ and 8.8 Hz, CH_2), 4.04 (bs, 1H, OH), 4.29–4.42 (m, 1H, CH), 7.52–7.65 (m, 5H, ArH); ^{13}C NMR ($CDCl_3$): δ 23.35 (CH_3), 62.84 (CH_2), 62.91 (CH), 124.05 (C-Ar), 129.37 (C-Ar), 130.99 (C-Ar), 143.13 (C-Ar). Found C, 59.05; H, 6.69; $C_9H_{12}O_2S$ requires C, 58.70; H, 6.53%.

The following β-hydroxy sulfoxides were synthesized similarly.

(*S*,*R*$_s$)-1-Phenylsulfinyl-2-propanol 4a: white solid; yield = 40%; mp 122–123°C (CH_2Cl_2/hexane); $[\alpha]_D^{27}=+369$ (*c* 0.75, CH_2Cl_2). The spectroscopic data (^1H NMR, ^{13}C NMR, MS) of (*S*,*R*$_s$)-**4a** is identical with (*R*,*S*$_s$)-**4a**.

(*R*,*S*$_s$)-1-(4-Methylphenylsulfinyl)-2-propanol 4b: white solid; yield = 38%; mp: 122–123°C (CH_2Cl_2/ hexane); $[\alpha]_D^{27}=-343$ (*c* 0.60, CH_2Cl_2); MS (*m*/*z*): 198 (M^+), 137, 123, 91, 83, 71 (100); ^1H NMR ($CDCl_3$): δ 1.23 (d, 3H, $J=6.4$ Hz, CH_3), 2.43 (s, 3H, CH_3), 2.61 (dd, 1H, $J=13.5$ and 1.7 Hz, CH_2), 3.09 (dd, 1H, $J=13.8$ and 9.6 Hz, CH_2), 3.91 (d, 1H, 2.9 Hz, OH), 4.31–4.38 (m, 1H), 7.37 (d, 2H, $J=8.1$ Hz, ArH), 7.53 (d, 2H, $J=8.2$ Hz, ArH); ^{13}C NMR ($CDCl_3$): δ 21.33 (CH_3), 23.25 (CH_3), 62.43 (CH_2), 64.02 (CH), 123.93 (C-Ar), 130.00 (C-Ar), 139.68 (C-Ar), 141.46 (C-Ar). Found C, 60.86; 7.42 H; $C_{10}H_{14}O_2S$ requires C, 60.61; H, 7.07%.

(*S*,*R*$_s$)-1-(4-Methylphenylsulfinyl)-2-propanol 4b: white solid; yield = 39%; mp: 122–123°C (CH_2Cl_2/hexane); $[\alpha]_D^{27}=+343°$ (*c* 0.50, CH_2Cl_2). The spectroscopic data (^1H NMR, ^{13}C NMR, MS) of (*S*,*R*$_s$)-**4b** is identical with (*R*,*S*$_s$)-**4b**.

Acknowledgements

We thank CSIR (India) for financial assistance, Dr. J. S. Rao (Novo Nordisk, India) for HLL and lipozyme samples and Professor V.S. Parmar for gift of lipases. S.S. thanks Professor Harjit Singh for financial support.

References

1. (a) Coppola, G. M.; Schuster, H. F. *α-Hydroxy Acids in Enantioselective Synthesis*; John Wiley & Sons: New York, 1997; (b) Wipf, P. In *Comprehensive Organic Synthesis*; Trost, B. M.; Flemming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 5, p. 827; (c) Agar, D. J.; Prakash, I.; Schaad, D. R. *Chem. Rev.* **1996**, *96*, 835; (d) Seyden-Penne, J. In *Chiral Auxiliaries and Ligands in Asymmetric Synthesis*; Wiley: New York, 1995; (e) Morrison, J. D. In *Asymmetric Synthesis*; Academic Press: New York, 1984.

2. (a) Laumen, K.; Breitgoff, D.; Schneider, M. P. *J. Chem. Soc., Chem. Commun.* **1988**, 1459; (b) *The Chemistry of Sulfur Containing Functional Groups*; Patai, S.; Rappoport, Z. Eds.; Wiley Interscience: New York, 1993; (c) Whithan, G. H. *Organosulfur Chemistry*; Oxford Science Publications: Oxford, 1995.
3. Liu, H.; Cohen, T. *J. Org. Chem.* **1995**, *60*, 2022.
4. (a) Fujisawa, T.; Itoh, T.; Nakai, M.; Sato, T. *Tetrahedron Lett.* **1985**, *26*, 771; (b) Goergens, U.; Schneider, M. P. *J. Chem. Soc., Chem. Commun.* **1991**, 1064; (c) Sanchez-Obregon, R.; Ortiz, B.; Walls, F.; Yuste, F.; Ruano, J. L. G. *Tetrahedron: Asymmetry* **1999**, *10*, 947.
5. Dinunno, L.; Franchini, C.; Nacci, A.; Scilimati, A.; Sinicropi, M. S. *Tetrahedron: Asymmetry* **1999**, *10*, 1913.
6. (a) Gruttadauria, M.; Meo, P.; Noto, R. *Tetrahedron* **1999**, *55*, 4769; (b) Gruttadauria, M.; Meo, P.; Noto, R. *Tetrahedron* **1999**, *55*, 1409.
7. Nakatsuka, T.; Iwata, H.; Tanaka, R.; Imajo, S.; Ishiguro, M. *J. Chem. Soc., Chem. Commun.* **1991**, 662.
8. (a) Crumbie, R. L.; Deol, B. S.; Nemorin, J. E.; Ridley, D. D. *Aust. J. Chem.* **1978**, *31*, 1965; (b) Cohen, T.; Tong, S. *Tetrahedron* **1997**, *53*, 9487.
9. Tranchier, J.-P.; Ratovelomanana-Vidal, V.; Genet, J.-P.; Tong, S.; Cohen, T. *Tetrahedron Lett.* **1997**, *38*, 2951.
10. (a) Fuganti, C.; Pedrocchi, F.; Giuseppe, S. S. *Chem. Lett.* **1990**, *7*, 1137; (b) Kim, B. M.; Lee, H.-Y.; Munson, P. M.; Guare, J. P.; McDonough, C. *Tetrahedron Lett.* **1993**, *34*, 6517–6520; (c) Shimizu, M.; Kouki, S.; Fujisawa, T. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 2655; (d) Kanvera, L. T.; Sundholm, O. *J. Chem. Soc., Perkin Trans. 1* **1993**, 2407; (e) Itoh, T.; Kuroda, K.; Tomosada, M; Takagi, Y. *J. Org. Chem.* **1991**, *56*, 797 and Ref. 4b.
11. (a) Sato, T.; Ito, T.; Fujisawa, T. *Tetrahedron Lett.* **1987**, *28*, 5677; (b) Solladie, G.; Wilb, N.; Bauder, C. *Tetrahedron Lett.* **2000**, *28*, 4189; (c) Naka, T.; Minakawa, N.; Kaga, D.; Matsuda, A. *J. Am. Chem. Soc.* **2000**, *122*, 7233; (d) Raghavan, S.; Rasheed, M. A.; Joseph, S. C.; Rajebder, A. *J. Chem. Soc., Chem. Commun.* **1999**, 1845; (e) Solladie, G.; Hutt, J.; Frechou, C. *Tetrahedron Lett.* **1987**, *28*, 61; (f) Solladie, G.; Frechou, C.; Hutt, J.; Demailly, G. *Bull. Soc. Chim. Fr.* **1987**, 827; (g) Solladie, G.; Fernandez, I.; Maestro, M. C. *Tetrahedron Lett.* **1991**, *32*, 509; (h) Piesler, B.; Rohmer, M. J. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2449.
12. (a) Arsenio, G.; Aleman, P. A.; Domingo, L. R.; Medico-Simón, M. *Tetrahedron Lett.* **1998**, *39*, 3277; (b) Eames, J.; Nekula, W. *Tetrahedron: Asymmetry* **2001**, *12*, 1 and references cited therein; (c) Arsenio, G.; Gaviña, P.; Cuena, A.; Ramirez de Arellano, M. C.; Domingo, L. R.; Medico-Simón, M. *Tetrahedron: Asymmetry* **2000**, 11, 3481.
13. (a) Solladié, G.; Carreño, M. C. *Organosulfur Chemistry*; Academic Press Ltd, 1995; pp. 1–47; (b) Drabowicz, J.; Kielbasinski, P.; Mikolajczyk, M. In *The Synthesis of Sulphones, Sulphoxides and Cyclic Sulphides*; Patai, S.; Rappoport, Z. Eds. John wiley & Sons; Chapters 3 and 4, 1994; (c) Carreño, M. C. *Chem. Rev.* **1995**, *95*, 1717; (d) Bertus, P.; Phansarath, P.; Ratovelomanaanividal, V.; Genet, J. P.; Touati, A. R.; Homri, T.; Barhassine, B. *Tetrahedron Lett.* **1999**, *40*, 3175; (e) Ogura, K.; Ishida, M.; Fujita, M. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 3987; (f) Bueno, A. B.; Carreno, M. C.; Ruano, J. L. G.; Pena, B.; Rubio, A.; Hoyos, M. A. *Tetrahedron* **1994**, *50*, 9355; (g) Solladié, G.; Hanquet, G.; Roland, C. *Tetrahedron Lett.* **1999**, *40*, 177; (h) Carreño, M. C.; Ruano, J. L. G.; Ana, M. M.; Concepcion, P.; Rodriguez, J. H.; Rubino, A.; Sanchez, J.; Solladié, G. *J. Org. Chem.* **1990**, *55*, 2120 references cited therein; (i) Solladié, G.; Colobert, F.; Denni, D. *Tetrahedron: Asymmetry* **1998**, *9*, 3081.
14. Paule, S. D. D.; Piombo, L.; Ratovelomanana-Vidal, V.; Greck, C.; Genet, J.-P. *Eur. J. Org. Chem.* **2000**, 1535.
15. (a) Andersen, K. K. *Tetrahedron Lett.* **1962**, 93; (b) For a modern version, see: Solladie, G.; Hutt, J.; Giradin, A. *Synthesis* **1987**, 173.
16. Singh, S.; Kumar, S.; Chimni, S. S. *Biotechnol. Lett.* **2000**, *22*, 1237.
17. To a stirred solution of L-(+)-*O*-acetylmandelic acid (AMA) (29 mg, 0.15 mmol) and 4-(*N*,*N*-dimethylamino)pyridine (4 mg, 0.03 mmol) and dicyclohexylcarbodiimide (31 mg, 0.15 mmol) in dry dichloromethane (2 mL) at 0°C was added (*R*)- or (*S*)- alcohol (0.11 mmol). After usual work up and recording of ^{1}H NMR of the crude diastereomeric ester, e.e. was calculated from integration of the methine protons. (Whitesell, J. K.; Reynolds, D. *J. Org. Chem.* **1983**, *48*, 3548).
18. See Ref. 12c for data of (R,R_s)-**4b**. For configurational assignments of β-hydroxy sulfoxides, see: (a) Kingsburry, C. A.; Auerbach, R. A. *J. Org. Chem.* **1971**, *36*, 1737; (b) Solladie, G.; Fernandez, I.; Maestro, C. *Tetrahedron Lett.* **1991**, *32*, 509; (c) Alvarez-Ibara, C.; Cuervo-Rodriguez, R.; Fernandez-Monreal, M. C.; Ruiz, M. P. *J. Org. Chem.* **1994**, *59*, 7284; (d) Alcudia, F.; Brunet, E.; Ruano, J. L. G.; Hoyos, M. A.; Prados, P.; Rodriguez, J. H. *Org. Magn. Resonance* **1983**, *21*, 643. Also see Refs. 7 and 13h cited therein.