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# Highly enantioselective kinetic resolution of *trans*-2-(phenylthio)cyclohexanol derivatives by immobilized *Candida antartica* B lipase

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ABSTRACT

*Candida antartica* B (immobilized CAL-B) mediated resolutions of *trans*-2-(phenylthio)cyclohexanol derivatives using vinyl acetate as acylating agent and MTBE as solvent provide excellent enantioselectivity (up to >99%) and high yield of both the enantiomers in short reaction time.



## 1. Introduction

Organosulfur compounds are of great significance in synthetic organic chemistry as they are widely used for the synthesis of potentially bioactive molecules, which find applications as agrochemicals [1], pharmaceuticals [2–4], chiral auxiliaries for analytical as well as synthetic applications [6–8] and in numerous selective organic synthesis [5].

Chiral hydroxy sulfides occupy a special place among the enantiopure organosulfur compounds, since the sulfur atom placed at an appropriate position from the hydroxy group provides unique synthetic versatility. Hence, they can be used as synthons for a variety of chiral organic compounds, such as chiral oxiranes [9], allylic alcohols [10], lactones [11], macrolides [12], pheromones [13] and tetrahydrofurans [14]. In particular, the asymmetric motifs obtained from relatively rigid cyclic structures, cyclic β-hydroxy sulfides have been employed as organocatalysts in Baylis–Hillman reaction [15]. Their transformation to hydroxy sulfoxides [16] or sulfones [17], provides useful chiral building blocks and chiral ligands, for example, β-hydroxy sulfoxides have been used as chiral ligands in the enantioselective addition of diethylzinc to benzaldehyde [18] and also in the synthesis of naturally occurring compounds such as leukotrienes [19].

Due to the importance of chiral β-hydroxy sulfides a number of methods have been developed for their synthesis such as; asymmetric ring opening of epoxides [20], asymmetric reduction of β-ketosulfides using Baker's yeast [21] and fungal whole cells [22], and kinetic resolution of racemic β-hydroxy sulfides with chiral 1,2-diamines [23] and enzymes [24,25]. The requirement of expensive or toxic metal catalysts [26], long reaction times [27], elevated temperature [28] and difficulty in handling cell mass in the above mentioned methods and our interest in the kinetic resolution [29] lead us to seek an effective and environmentally benign approach for the synthesis of enantiomerically pure *trans*-2-(phenylthio)cyclohexanol derivatives.

The enantioselective kinetic resolution of secondary alcohols with lipases provides an environmentally benign approach to obtain optically pure alcohols. Herein we report our results on the lipase mediated kinetic resolution of *trans*-2-(phenylthio)cyclohexanol derivatives and their functionalization to optically pure β-hydroxy sulfoxides.

## 2. Results and discussions

In the preliminary study, *Humicola lanuginosa* lipase was used to resolve *trans*-2-(phenylthio)cyclohexanol, (±)-**1** using vinyl acetate as acylating agent under solvent free conditions at room temperature (Scheme 1). The progress of the reactions was monitored at regular intervals for 24 h by chiral HPLC using chiralcel OD-H column (Fig. 1, Table 1, entry 1).

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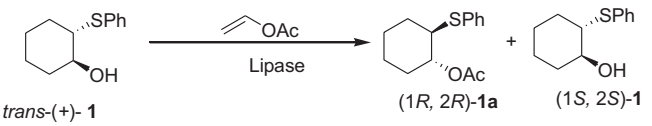



**Scheme 1.** Lipase mediated kinetic resolution of *trans*-2-(phenylthio)cyclohexanol, (±)-**1**.

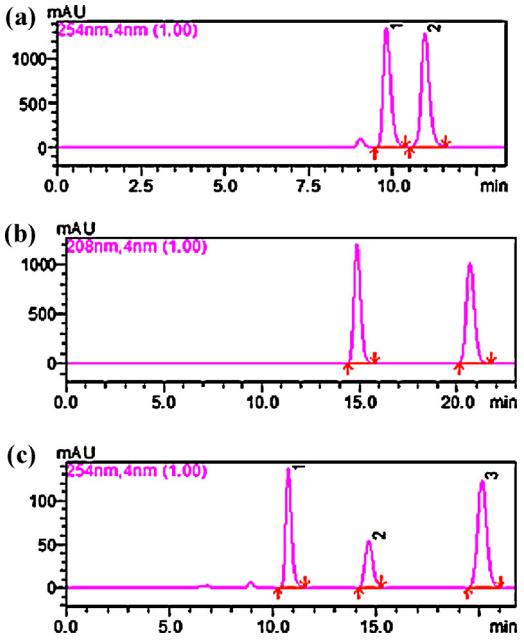



**Fig. 1.** An overlay of HPLC traces of (a) racemic acetylated product, **1a**; (b) racemic alcohol, (±)-**1**; (c) after resolution of 24 h with HLL lipase.

After workup and purification on silica gel column, the acetylated product, (1*R*, 2*R*)-**1a** was obtained in >99% enantiomeric excess and the unreacted alcohol, (1*S*, 2*S*)-**1** was obtained with 55% ee (Table 1, entry 1). Similarly other lipases were screened for resolution of *trans*-2-(phenylthio)cyclohexanol [(±)-**1**]. Most of the lipases were found to be less efficient in resolving (±)-**1** but *Burkholderia cepacia* lipase resolved the substrate in 8 h to provide **1a** in >99% ee and **1** in 90% ee (Table 1 entry 8). *Candida antartica* B lipase (CAL B) was found to be most efficient in resolving (±)-**1** in 4 h to provide (1*R*, 2*R*)-**1a** in >99% ee and (1*S*, 2*S*)-**1** in 92% ee (Table 1 entry 5), so it was selected for further optimization.

Further, the effect of different solvents was studied on the resolution of (±)-**1** by CAL-B. The reaction was performed by using 1 mL solvent (Table 2). It was observed that polar solvents result in a lower conversion of (±)-**1** as well as lower enantioselectivity of (1*S*, 2*S*)-**1** in comparison to non-polar solvents. The reaction run in methyl *tert*-butyl ether (MTBE) resolved both the products with >99% ee while the conversion was observed at 50%. Thus, MTBE (1 mL) was added in all further optimization reactions. The study for time of resolution was carried out in order to obtain the exact time in which 50% of resolution was achieved. It was observed that enantioselectivity of (1*R*, 2*R*)-**1a** and conversion increase with reaction time till 4 h and no further change was observed (Fig. 2, graph I). So, the reaction time of 4 h was taken as optimum.

Next, the variation in the amount of vinyl acetate for kinetic resolution of (±)-**1** was studied, the results illustrated in Fig. 2. Both the resolved products (1*R*, 2*R*)-**1a** and (1*S*, 2*S*)-**1** were obtained in >99% ee on using 10 equiv. of the vinyl acetate with respect to 1 equiv. of the substrate. Using lower amounts of vinyl acetate provided products with slightly lower enantiomeric excess. So, 10 equiv. of vinyl acetate was used for all further optimizations (Fig. 2, graph IV). The optimization for amount of lipase with respect to substrate was studied by varying lipase-substrate ratios (w/w) from 0.2 to 2.00 (Fig. 2, graph III). It was found that conversion as well as enantioselectivity increases from 0.2 to 1.00 of lipase:substrate ratio while the lipase substrate ratio 1:1 was optimum to achieve 50% conversion and obtained (1*R*, 2*R*)-**1a** and (1*S*, 2*S*)-**1** in >99% ee. There was no change in results using higher amounts of lipase with respect to substrate. Since, enzyme catalysis is sensitive to changes in temperature, thus the reaction was performed at different temperatures. It was found that the best results, i.e. >99% ee for both (1*R*, 2*R*)-**1a** and (1*S*, 2*S*)-**1** with 50% conversion was obtained on running the reaction at temperatures 30 °C and 40 °C (Fig. 2, graph II). The reaction temperature of was selected for running all further reactions.

Thus, the optimized condition for the resolution of *trans*-2-(phenylthio)cyclohexanol (±)-**1** consist of stirring a mixture of (±)-**1** (100 mg) in MTBE (1 mL) and vinyl acetate (412 μL, 10 equiv.) with CAL-B (100 mg) as the catalyst (Scheme 2). Further, the scope of this resolution was observed by screening different derivatives of *trans*-2-(phenylthio)cyclohexanol using the optimized conditions (Table 3, entry 1–13).

**Table 2**
Solvent screening for resolution of *trans*-2-(Phenylthio)cyclohexanol.

| S. no. | Solvent | Conversion (%) | $ee_p$ [a] (%) | $ee_s$ [a] (%) | $E$ [b] |
|---|---|---|---|---|---|
| 1 | NEAT | 50 | >99 | 92 | >500 |
| 2 | THF | 37 | >99 | 64 | >500 |
| 3 | DCM | 48 | >99 | 86 | >500 |
| 4 | Hexane | 43 | >99 | 97 | >500 |
| 5 | Acetonitrile | 48 | >99 | 95 | >500 |
| 6 | MTBE | 50 | >99 | >99 | >500 |
| 7 | Toluene | 30 | 71.5 | 37 | 8 |
| 8 | Dioxane | 41 | 81 | 69 | 19 |
| 9 | Ethyl acetate | 18 | >99 | 26 | 66 |
| 10 | Methanol | 10 | >99 | 14 | 87 |
| 11 | DMSO | 11 | >99 | 16.5 | 63 |
| 12 | DMF | 9 | >99 | 69 | >500 |
| 13 | Dichloroethane | 24 | >99 | 61 | >500 |

[a] $ee_s$ and $ee_p$ are calculated from HPLC.
[b] $E = \ln[(1-c)(1-ee_s)]/\ln[(1-c)(1+ee_s)]$ where $c = ee_s/ee_s + ee_p$.

**Table 1**
Results of lipases screening for resolution of *trans*-2-(phenylthio)cyclohexanol.

| S. no. | Lipase | Conversion (%) | Time taken (h) | $ee_p$ [a] (%) | $ee_s$ [a] (%) | $E$ [b] |
|---|---|---|---|---|---|---|
| 1 | *Humicola lanuginosa* | 34 | 24 | 99 | 55 | 155 |
| 2 | *Pseudomonas stutzeri* | 46 | 24 | >99 | 82 | >500 |
| 3 | *Pseudomonas fluorescens* | 39 | 24 | >99 | 65 | 238 |
| 4 | *Candida rugosa* | 11 | 24 | 99 | 15 | 604 |
| 5 | *Immobilized Candida antartica B* | 50 | 4 | >99 | 92 | >500 |
| 6 | *Aspergillus niger* | 31 | 24 | 99 | 50 | 110 |
| 7 | *Burkholderia cepacia* | 18 | 24 | 99 | 29 | 10 |
| 8 | *Burkholderia cepacia* (immobilized on ceramic) | 48 | 8 | >99 | 90 | 246 |
| 9 | *Burkholderia cepacia* (immobilized diatomite) | 48 | 8 | >99 | 89 | 246 |

[a] $ee_s$ and $ee_p$ are calculated from HPLC.
[b] $E = \ln[(1-c)(1-ee_s)]/\ln[(1-c)(1+ee_s)]$ where $c = ee_s/ee_s + ee_p$.

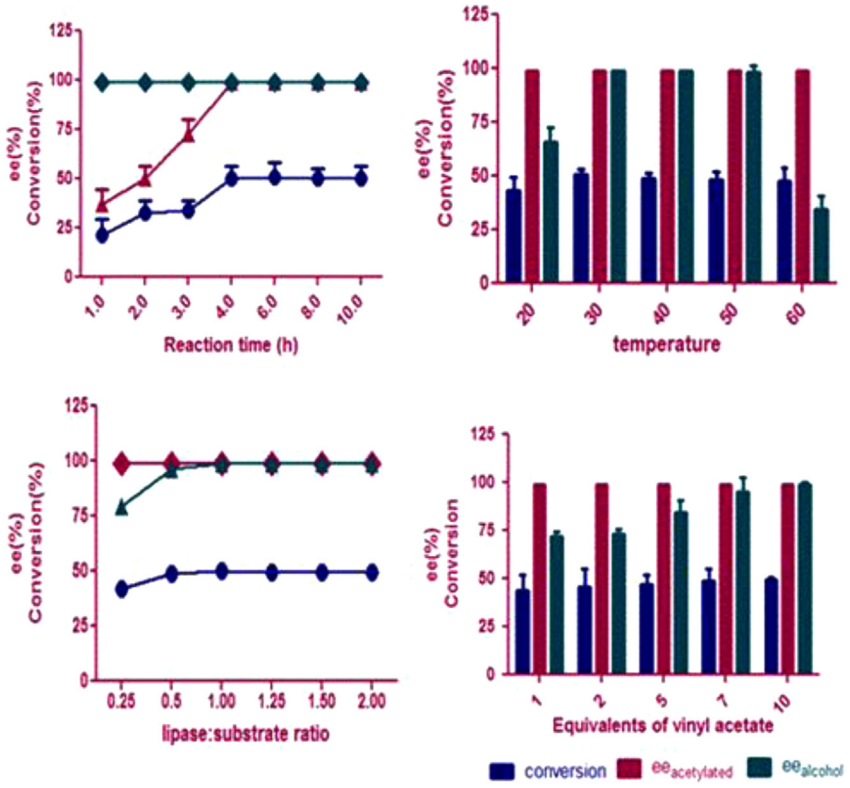



**Fig. 2.** Optimizing reaction conditions: (I) reaction time; (II) Temperature; (III) lipase-substrate ratio; (IV) equivalents of vinyl acetate.

It had been observed that conversion of 50% and >99% enantioselectivity with $E > 500$ was achieved for both the acetylated and unreacted enantiomers in all substrates ranging from 1 to 13. However, a slight variation in reaction times (3–9 h) was observed. It has been found that the resolution of *trans*-2-(phenylthio)cyclohexanol (Table 3, entry 1) can be obtained with >99% ee in 4 h while the *trans*-2-(phenylthio)cyclopentanol (Table 3, entry 11) was resolved in 3 h affording (1*R*, 2*R*)-2-(phenylthio)cyclopentyl acetate and(1*S*, 2*S*)-2-(phenylthio)cyclopentanol in >99% ee. Varying the substitution at phenyl ring of the thiol part of the molecule, it was observed that *p*-halo substituted β-hydroxy sulfides took longer time for the transformation than *p*-methyl- and *p*-methoxy-substituted derivatives. However, the substitution pattern of *ortho*-, *meta*- and *para*- was studied by using the three derivatives of *trans*-2-(chlorophenylthio)cyclohexanol (Table 3, entry 2, 3, 4). It was observed that *ortho* substituted derivative took 9 h to resolve while *meta* and *para* were resolved in 7 h and 6 h, respectively. *trans*-2-(Cyclohexylthio)cyclohexanol provided the corresponding acetate and alcohol in 50% conversion in 8 h (Table 3, entry 10). However, the acyclic hydroxy sulfides (Table 3, entry 12 and 13) undergo resolution with >99% ee of both the products in 4 h and 5 h, respectively.

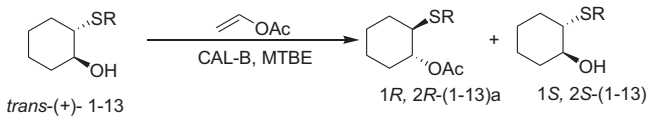
Further, sulfoxidation of the isolated enantiopure (1*R*, 2*R*)-**1a** and (1*S*, 2*S*)-**1** was studied with *m*-CPBA in $CH_2Cl_2$ at −20 °C (Scheme 3). The oxidation of (1*R*, 2*R*)-**1a** provided a mixture of (1*R*, 2*R*, $S_s$)- and (1*R*, 2*R*, $R_s$)-2-(phenylsulfinyl)cyclohexyl acetate **14a**. The fractional crystallization of this diastereomeric mixture provided (1*R*, 2*R*, $S_s$)-**14a** as pure colorless crystals (>99% ee, m.p. 153 °C) having $[\alpha]_D^{27} = +112.9°$ (c 0.50, $CH_2Cl_2$) and mother liquor (**14a**) as a colorless liquid with $[\alpha]_D^{27} = -110.0°$ (c 1.0, $CH_2Cl_2$). The crystalline diastereomer (1*R*, 2*R*, $S_s$)-**14a** was assigned the configuration on the basis of its X-ray data (Fig. 2) as well on comparison of the specific rotation values as reported in literature [30].

Similarly oxidation of (1*S*, 2*S*)-2-(phenylthio)cyclohexanol (**1**) followed by crystallization afforded (1*S*, 2*S*, $S_s$)-**14** and (1*S*, 2*S*, $R_s$)-**14** (>99% ee, mp: 156 °C) having $[\alpha]_D^{27} = -129.2$ (c 1.0, $CH_2Cl_2$) (Table 4).

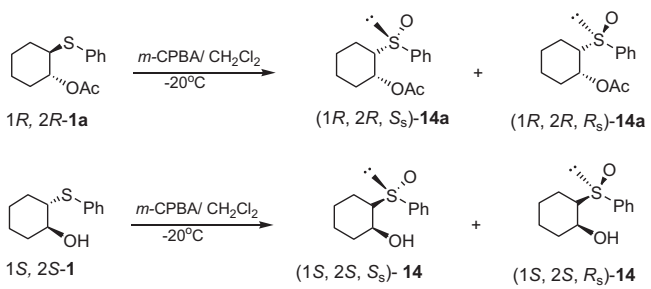
The absolute configurations of the sulfoxides have been assigned on the basis of X-ray data [31] (Fig. 3) as well as the specific rotation values compared to literature [30].

### 2.1. Reusability of enzyme

The lipase reused for next cycle was filtered from the previous reaction, washed with ethyl acetate, dried and the weighed. For carrying out the next cycle, the amount of substrate was taken with respect to the amount of enzyme recovered from earlier cycle,




**Scheme 2.** Optimized condition for carrying out resolution of different derivatives of *trans*-2-(phenylthio)cyclohexanol.




**Scheme 3.**

**Table 3**
Kinetic resolution of different derivatives of β-hydroxy sulfides with *Candida antartica* lipase B.

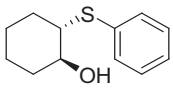
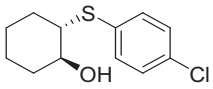
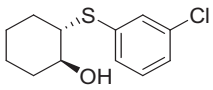
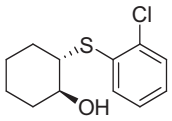
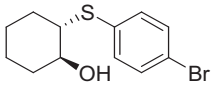
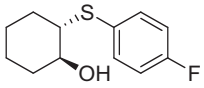
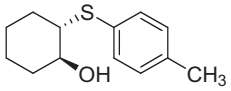
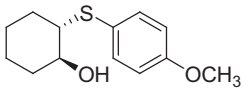
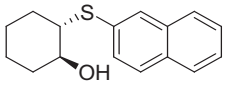
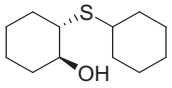
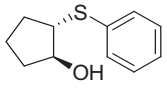
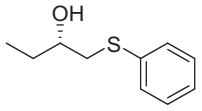
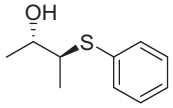
| Entry | Substrate *trans*-(±)-1-13 | Reaction time (h) | Conv (%) | (1-13)a | | (1-13) | | *E* |
|---|---|---|---|---|---|---|---|---|
| | | | | $ee_p$ (%) | Yield (%) | $ee_s$ (%) | Yield (%) | |
| 1 |  | 4 | 50 | >99 | 42 | >99 | 46 | >500 |
| 2 |  | 6 | 50 | >99 | 47 | >99 | 37 | >500 |
| 3 |  | 7 | 48 | >99 | 42 | >99 | 44 | >500 |
| 4 |  | 9 | 48 | >99 | 47 | >99 | 42 | >500 |
| 5 |  | 5 | 50 | >99 | 35 | >99 | 41 | >500 |
| 6 |  | 8 | 47 | >99 | 44 | >99 | 41 | >500 |
| 7 |  | 5 | 50 | >99 | 45 | >99 | 43 | >500 |
| 8 |  | 6 | 50 | >99 | 47 | >99 | 42 | >500 |
| 9 |  | 6 | 50 | >99 | 46 | >99 | 40 | >500 |
| 10 |  | 8 | 47 | >99 | 38 | >99 | 35 | >500 |
| 11 |  | 3 | 50 | >99 | 43 | >99 | 45 | >500 |
| 12 |  | 4 | 50 | >99 | 40 | >99 | 44 | >500 |
| 13 |  | 5 | 50 | >99 | 41 | >99 | 46 | >500 |

**Table 4**
β-Hydroxy sulfoxides obtained from chiral products of β-hydroxy sulfide (**1**).

| β-Hydroxy sulfide | β-Hydroxy sulfoxide | m.p. (°C) | $[\alpha]_D^{27}$ | ee (%) |
|---|---|---|---|---|
| (1*R*, 2*R*)-1a | (1*R*, 2*R*, $S_s$)-14a | 153–156 | +112.9 (*c* = 0.50, $CH_2Cl_2$). | >99 |
| (1*R*, 2*R*)-1a | (1*R*, 2*R*, $R_s$)-14a | – | −110.0 (*c* = 1.0, $CH_2Cl_2$). | >99 |
| (1*S*, 2*S*)-1 | (1*S*, 2*S*, $S_s$)-14 | 156–157 | −129.2 (*c* = 1.0, $CH_2Cl_2$) | >99 |
| (1*S*, 2*S*)-1 | (1*S*, 2*S*, $R_s$)-14 | – | +132.1 (*c* = 0.75, $CH_2Cl_2$) | >99 |

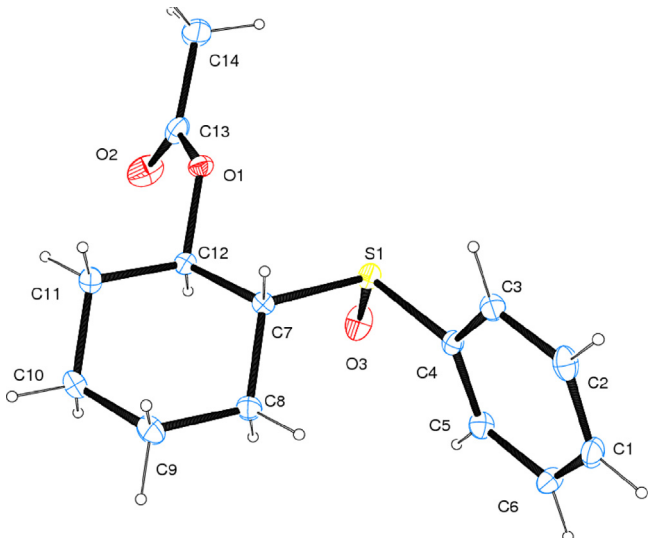



**Fig. 3.** X-ray structure of **14a**.

**Table 5**
Reusability of enzyme up to 4 cycles.

| Entry | Cycle | Time taken (h) |
|---|---|---|
| 1 | 1st | 4 |
| 2 | 2nd | 12 |
| 3 | 3rd | 24 |
| 4 | 4th | 32 |

maintaining the enzyme-substrate ratio 1:1. Immobilized CAL-B gave reproducible results with 50% conversion and >99% enantioselectivity for the kinetic resolution of (±)-**1a** with vinyl acetate in MTBE over the four reuse cycles investigated. The same enantioselectivity and conversion was observed over the four sequentially performed reactions, however the time taken to achieve 50% conversion was longer. The second cycle requires 12 h in order to reach the full 50% conversion instead of 4 h in the first cycle while the third cycle requires almost 24 h to achieve complete conversion. The slow rate of conversion could be attributed to the possible leaching of the enzyme [32] from the immobilization support (acrylic resin) (Table 5).

## 3. Conclusions

In this study, a series of β-hydroxy sulfides were successfully resolved with excellent enantioselectivity (up to ≥99% ee) via immobilized CAL-B catalyzed kinetic hydrolysis of the corresponding β-hydroxy phenylthiocyclohexanols. The method developed is simple, environmentally benign and highly enantioselective.

## 4. Experimental

### 4.1. Materials and methods

NMR spectra were obtained at 300 MHz (JEOL AL-300) using either $CDCl_3$ or DMSO as solvents with $Me_4Si$ in $CDCl_3$ as the internal standard. The chemical shifts are given in delta ($\delta$) values and the coupling constants ($J$) in Hertz (Hz). Spectral patterns are designated as s = singlet; d = doublet; dd = doublet of doublets; q = quartet; t = triplet; br = broad; m = multiplet. Analytical thin layer chromatography (TLC) was performed on either (i) aluminum sheets pre-coated with silica gel GF254 (Merck, India) or (ii) glass plates (7.5 cm × 2.5 cm) coated with silica gel GF-254 (Spectrochem, India). Visualization of the spots was accomplished by exposing to UV light or iodine vapors. Column chromatography was performed using silica gel 60–120 and 100–200. HPLC analyses were carried out in a Hewlett Packard 1100 chromatograph, UV detector using a SPD-M20A prominence diode array detector (25 cm × 4.6 mm), Daicel Chiralpak OD-H (25 cm × 4.6 mm), Chiralpak AS-H (25 cm × 4.6 mm), Chiralcell IB (25 cm × 4.6 mm) columns, varying the conditions according to the specific substrate. Measurements of the optical rotation values were done in a PerkinElmer 241 polarimeter.

### 4.2. General method for preparation of substrates

To a stirred solution of epoxide (3 mmol) and potassium carbonate (0.04 g) in a round bottom flask was added water (2 mL) and corresponding thiophenol (3 mmol) and the resulting mixture was stirred at room temperature for 30–240 min. In case of solid β-hydroxy sulfides, pure product was isolated by filtration. The liquid β-hydroxy sulfides were extracted with ethyl acetate and dried over anhydrous sodium sulphate. Evaporation of solvent under reduced pressure afforded pure product.

***trans*-(±)-2-(Phenylthio)cyclohexanol (1)**: Yield: 82%, White solid $^1$H NMR ($CDCl_3$, 300 MHz), $\delta$ [ppm]: 1.23–1.35 (m, 4H), 1.66–1.70 (m, 2H), 2.07–2.11 (m, 1H), 2.95 (m, 1H), 7.24–7.31 (m, 3H), 7.44–7.48 (m, 2H); $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ [ppm]: 24.2, 26.1, 32.7, 33.8, 56.5, 72.1, 127.7, 128.8, 133.7; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 0.5 mL/min, 220 nm, retention time: 14.89 min (1*R*, 2*R*), 21.66 (1*S*, 2*S*) min; HRMS (M+Na) calcd. for $C_{12}H_{16}OS$: 231.0838, found: 231.0814.

***trans*-(±)-2-(*p*-Tolylthio)cyclohexanol (2)**: Yield: 79%; $^1$H NMR ($CDCl_3$, 300 MHz), $\delta$ [ppm]: 1.20–1.33 (m, 4H), 1.59–1.72 (m, 2H), 2.05–2.14 (m, 2H), 2.34 (s, 3H) 2.63–2.70 (m, 1H), 3.04–3.29 (m, 1H), 7.10–7.25 (m, 2H), 7.35–7.38 (m, 2H); $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ [ppm]: 24.2, 26.1, 32.7, 33.8, 56.5, 72.1, 127.7, 128.8, 133.7; HPLC analysis: Daicel Chiralcel OD-H, hexane/i-PrOH = 9/1, flow rate = 0.5 mL/min, 220 nm, retention time: 11.23 min (1*R*, 2*R*), 18.72 min (1*S*, 2*S*); HRMS (M+Na) calcd. for $C_{13}H_{18}OS$: 245.0974, found: 245.0971.

***trans*-(±)-2-(4-Chlorophenylthio)cyclohexanol (3)**: Yield: 83%; $^1$H NMR ($CDCl_3$, 300 MHz), $\delta$ [ppm]: 1.23–1.27 (m, 1H), 1.66–1.70 (m, 2H), 2.07–2.11 (m, 1H), 2.95 (m, 1H), 7.24–7.31 (m, 5H), 7.44–7.48 (m, H); $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ [ppm]: 20.9, 23.4, 24.9, 31.3, 31.5, 50.2, 75.2, 126.8, 129.6, 129.7, 131.1; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 1.0 mL/min, 220 nm, retention times: 9.45 min (1*R*, 2*R*), 13.26 min (1*S*, 2*S*); HRMS (M+Na) calcd. for $C_{12}H_{15}ClOS$: 265.0453, found: 265.0452.

***trans*-(±)-2-(3-Chlorophenylthio)cyclohexanol (4)**: Yield: 74%; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 1.0 mL/min, 220 nm, retention time: 8.56 min (1*R*, 2*R*), 11.55 min (1*S*, 2*S*); HRMS (M+Na) calcd. for $C_{12}H_{15}ClOS$: 265.0442, found: 265.0447.

***trans*-(±)-2-(2-Chlorophenylthio)cyclohexanol (5)**: Yield: 77%; $^1$H NMR ($CDCl_3$, 300 MHz), $\delta$ [ppm]: 1.27–1.39 (m, 4H), 1.72–1.73 (m, 2H), 2.12–2.16 (m, 2H), 2.89–2.94 (m, 2H), 3.43 (m, 1H), 7.18–7.54 (m, 5H); $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ [ppm]: 24.1, 25.9, 32.4, 33.9, 55.8, 72.6, 127.0, 128.4, 129.9, 132.8, 133.9, 136.8. HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 1.0 mL/min, 220 nm, retention time: 10.13 min (1*R*, 2*R*), 12.40 min (1*S*, 2*S*); HRMS (M+Na) calcd. for $C_{12}H_{15}ClOS$: 265.0438, found: 265.0434.

***trans*-(±)-2-(4-Bromophenylthio)cyclohexanol (6)**: Yield: 89%; $^1$H NMR ($CDCl_3$, 300 MHz), $\delta$ [ppm]: 1.39 (m, 4H), 1.73 (m, 2H), 2.08 (m,2H), 3.18 (m, 1H), 4.78 (m, 1H), 7.19–7.30 (m, 4H); $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ [ppm]: 20.9, 23.4, 24.9, 31.3, 50.2, 75.2, 126.8, 129.7, 131.1, 134.3, 137.1. HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 0.3 mL/min, 220 nm, retention times:

15.24 min (1*R*, 2*R*), 20.33 min (1*S*, 2*S*); HRMS (M+Na) calcd. for $C_{12}H_{15}BrOS$: 309.0254, found: 309.0249.

***trans*-(±)-2-(4-Fluorophenylthio)cyclohexanol (7)**: Yield: 87%; $^1$H NMR ($CDCl_3$, 300 MHz), $\delta$ [ppm]: 1.20–1.34 (m, 6H), 1.66–1.74 (m, 2H), 2.03–2.15 (m, 1H), 2.66–3.28 (m, 1H), 6.98–7.04 (m, 2H), 7.44–7.48 (m, 2H); HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 0.5 mL/min, 254 nm, retention times: 14.98 min (1*R*, 2*R*), 17.20 min (1*S*, 2*S*); HRMS (M+K) calcd. for $C_{12}H_{15}FOS$: 265.1474, found: 265.1473.

***trans*-(±)-2-(4-Methoxyphenylthio)cyclohexanol (8)**: Yield: 75%; $^1$H NMR ($CDCl_3$, 300 MHz), $\delta$ [ppm]: 1.32–1.45 (m, 4H), 1.50–1.86 (m, 4H), 3.71 (s, 3H) 2.52–2.69 (m, 1H), 3.23–3.47 (m, 1H), 6.65–7.38 (m, 4H); $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ [ppm]: 21.7, 25.4, 28.2, 56.1, 61.9, 72.6, 114.7, 127.6, 128.9, 157.0; HPLC analysis: Daicel Chiralcel OD-H, hexane/*i*-PrOH = 9/1, flow rate = 0.5 mL/min, 220 nm, retention time: 12.13 min (1*R*, 2*R*), 17.82 min (1*S*, 2*S*); HRMS (M+Na) calcd. for $C_{13}H_{18}O_2S$: 261.3349, found: 261.3350.

***trans*-(±)-2-(Naphthalen-3-ylthio)cyclohexanol (9)**: Yield: 82%; $^1$H NMR ($CDCl_3$, 300 MHz), $\delta$ [ppm]: 1.27–1.39 (m, 4H), 1.72–1.73 (m, 2H), 2.12–2.16 (m, 2H), 2.89–2.94 (m, 2H), 3.43 (m, 1H), 7.18–7.54 (m, 5H); $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ [ppm]: 24.2, 26.1, 32.6, 33.8, 56.5, 72.1, 126.4, 126.5, 126.7, 127.4, 127.6, 128.4, 129.9, 130.9, 132.5, 132.7, 133.5; HPLC analysis: Daicel chiralpak AS-H, hexane/i-PrOH 97/3, 1.0 mL/min, 220 nm, retention time: 9.87 min (1*R*, 2*R*), 11.04 min (1*S*, 2*S*); 11.04 min; HRMS (M+Na) calcd. for $C_{16}H_{18}OS$: 281.0977, found: 281.0980.

***trans*-(±)-2-(Cyclohexylthio)cyclohexanol (10)**: Yield: 69%; $^1$H NMR ($CDCl_3$, 300 MHz), $\delta$ [ppm]: 1.37–1.46 (m, 10H), 1.47–1.92 (m, 6H), 2.48–2.56 (m,2H), 3.44 (m, 1H); $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ [ppm]: 24.2, 24.4, 25.2, 25.5, 26.1, 26.3, 26.4, 33.6,34.4, 34.6, 34.9, 37.8, 38.4, 43.63, 52.6, 72.5. HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 0.5 mL/min, 220 nm, retention time: 14.78 min (1*R*, 2*R*), 19.93 min (1*S*, 2*S*); HRMS (M+Na) calcd. for $C_{12}H_{22}OS$: 237.1247, found: 237.1239.

***trans*-(±)-2-(Phenylthio)cyclopentanol (11)**: Yield: 75%; $^1$H NMR ($CDCl_3$, 300 MHz), $\delta$ [ppm]: 1.59–1.80 (m, 6H), 3.39–3.40 (m, 1H), 4.10–4.12 (m, 1H), 7.20–7.42 (m, 5H); $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ [ppm]: 20.8, 28.2, 34.1, 47.9, 88.7, 125.4, 126.7, 129.2, 135.9; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 90/10, 0.5 mL/min, 220 nm, retention time: 10.35 min (1*R*, 2*R*), 12.51 min (1*S*, 2*S*); HRMS (M+K) calcd. for $C_{11}H_{14}OS$: 233.0630, found: 233.0632.

**(±)-1-(Phenylthio)butan-2-ol (12)**: Yield: 74%; $^1$H NMR ($CDCl_3$, 300 MHz), $\delta$ [ppm]: 0.94–0.99 (m, 2H), 1.49–1.61 (m, 3H), 2.80–2.88 (m, 1H), 3.12–3.18 (m, 1H), 3.56–3.64 (m, 1H), 7.18–7.39 (m, 5H); HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 0.5 mL/min, 220 nm, retention times: 9.78 min (*R*); 10.93 min (*S*); HRMS (M+K) calcd. for $C_{10}H_{14}OS$: 221.1160, found: 221.1159.

***trans*-(±)-3-(Phenylthio)butan-2-ol (13)**: Yield: 72%; $^1$H NMR ($CDCl_3$, 300 MHz), $\delta$ [ppm]: 1.22–1.29 (m, 6H), 3.04–3.09 (m, 1H), 3.66–3.68 (m, 1H), 7.25–7.64 (m, 5H); HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 0.5 mL/min, 220 nm, retention times: 9.43 min (1*R*, 2*R*), 11.80 min (1*S*, 2*S*); HRMS (M+K) calcd. for $C_{10}H_{14}OS$: 221.0621, found: 221.0623.

### *4.3. General method for preparation of racemic acetates*

To a stirred solution of β-hydroxy sulfide (1 equiv.), 5 equiv. of acetyl chloride was added at 0 °C. The reaction mixture was stirred at 0 °C for 10–30 min. The excess acetyl chloride was removed under reduced pressure. The racemic acetates were purified by column chromatography.

***trans*-(±)-2-(Phenylthio)cyclohexyl acetate (1a)**: Yield: 68%; $^1$H NMR ($CDCl_3$, 300 MHz), $\delta$ [ppm]: 1.39–1.50 (m, 4H), 1.55–1.87 (m, 4H), 2.01 (s, 3H), 3.07 (m, 1H), 4.18 (m, 1H), 7.02–7.18 (m, 5H); $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ [ppm]: 21.0, 21.6, 24.7, 28.2, 58.9, 70.3, 74.6, 125.2, 126.8, 129.0, 136.4; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 0.5 mL/min, 220 nm, retention time: 10.65 min (1*S*, 2*S*), 11.23 min (1*R*, 2*R*); HRMS (M+Na) calcd. for $C_{14}H_{18}O_2S$: 273.0913, found: 273.0912.

***trans*-(±)-2-(*p*-Tolylthio)cyclohexyl acetate (2a)**: Yield: 72%; $^1$H NMR ($CDCl_3$, 300 MHz), $\delta$ [ppm]: 1.32–1.47 (m, 4H), 1.53–1.87 (m, 4H), 2.01 (s, 3H), 2.35 (s, 1H), 3.07 (m, 1H), 4.18 (m, 1H), 6.92–7.10 (m, 4H); $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ [ppm]: 21.0, 21.6, 24.3, 28.2, 29.9, 58.9, 74.6, 126.7, 129.3, 133.4, 134.8, 170.3; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 0.5 mL/min, 220 nm, retention time: 5.94 min (1*S*, 2*S*), 6.63 min (1*R*, 2*R*); HRMS (M+Na) calcd. for $C_{15}H_{20}O_2S$: 287.1075 found: 287.1100.

***trans*-(±)-2-(4-Chlorophenylthio)cyclohexyl acetate (3a)**: Yield: 71%; $^1$H NMR ($CDCl_3$, 300 MHz), $\delta$ [ppm]: 1.31–1.49 (m, 4H), 1.57–1.92 (m, 4H), 2.01 (s, 3H), 3.07 (m, 1H), 4.18 (m, 1H), 7.12–7.24 (m, 4H); $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ [ppm]: 21.0, 21.6, 24.7, 28.2, 29.9, 58.9, 74.6, 128.2, 129.1, 130.7, 134.5, 170.3; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 1.0 mL/min, 220 nm, retention times: 5.05 min (1*S*, 2*S*), 5.78 min (1*R*, 2*R*).

***trans*-(±)-2-(3-Chlorophenylthio)cyclohexyl acetate (4a)**: Yield 67%; $^1$H NMR ($CDCl_3$, 300 MHz), $\delta$ [ppm]: 1.30–1.48 (m, 4H), 1.60–1.91 (m, 4H), 2.01 (s, 3H), 3.09 (m, 1H), 4.20 (m, 1H), 7.02–7.21 (m, 4H); $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ [ppm]: 21.2, 24.5, 28.0, 29.7, 58.4, 74.2, 124.9, 125.2, 130.5, 136.6, 170.1; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 1.0 mL/min, 220 nm, retention time: 4.80 min (1*S*, 2*S*), 5.14 min (1*R*, 2*R*).

***trans*-(±)-2-(2-Chlorophenylthio)cyclohexyl acetate (5a)**: Yield: 64%; $^1$H NMR ($CDCl_3$, 300 MHz), $\delta$ [ppm]: 1.32–1.47 (m, 4H), 1.59–1.89 (m, 4H), 2.12 (s, 3H), 3.09 (m, 1H), 4.16 (m, 1H) 6.92–7.22 (m, 4H); $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ [ppm]: 21.5, 22.0, 24.6, 28.0, 29.8, 58.4, 74.6, 126.6, 127.1, 128.9, 136.0, 170.4; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95:5, 1.0 mL/min, 220 nm, retention time: 3.69 min (1*S*, 2*S*), 4.36 min (1*R*, 2*R*).

***trans*-(±)-2-(4-Bromophenylthio)cyclohexyl acetate (6a)**: Yield: 84%; $^1$H NMR ($CDCl_3$, 300 MHz), $\delta$ [ppm]: 1.27–1.49 (m, 4H), 1.52–1.89 (m, 4H), 2.01 (s, 3H), 3.07 (m, 1H), 4.18 (m, 1H), 7.07–7.33 (m, 4H); $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ [ppm]: 21.0, 21.6, 24.7, 28.2, 29.9, 58.9, 74.6, 119.5, 129.0, 131.9, 135.4, 170.3; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95:5, 0.3 mL/min, 220 nm, retention time: 5.72 min (1*S*, 2*S*), 6.41 min (1*R*, 2*R*); HRMS (M+K) calcd. for $C_{14}H_{17}O_2BrS$: 369.0069, found: 368.0074.

***trans*-(±)-2-(4-Fluorophenylthio)cyclohexyl acetate (7a)**: Yield: 79%; $^1$H NMR ($CDCl_3$, 300 MHz), $\delta$ [ppm]: 1.25–1.43 (m, 4H), 1.58–1.71 (m, 2H), 1.97 (m,3H), 2.03–2.42 (m, 2H), 2.97–3.05 (m, 1H), 4.70–4.76 (m, 1H), 6.96–7.02 (m, 2H), 7.40–7.45 (m, 2H); $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ [ppm]: 21.1, 23.5, 25.0, 31.3, 31.5, 50.8, 74.8, 115.6, 115.9, 135.3, 135.4; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95:5, 0.5 mL/min, 254 nm, retention times: 10.45 min (1*S*, 2*S*), 11.50 min (1*R*, 2*R*); HRMS (M+Na) calcd. for $C_{14}H_{17}FO_2S$: 291.0929 found: 291.0933.

***trans*-(±)-2-(4-Methoxyphenylthio)cyclohexyl acetate (8a)**: Yield: 69%; $^1$H NMR ($CDCl_3$, 300 MHz), $\delta$ [ppm]: 1.37–1.48 (m, 4H), 1.55–1.85 (m, 4H), 2.03 (s, 3H), 3.01–3.10 (m, 1H), 4.09–4.20 (m, 1H), 3.69 (s, 3H), 6.65–7.10 (m, 5H); $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ [ppm]: 21.1, 22.6, 24.5, 28.0, 29.8, 55.4, 58.7, 74.4, 114.0, 127.5, 128.9, 156.9, 170.6; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 97/3, 1.0 mL/min, 220 nm, retention times: 3.58 min (1*S*, 2*S*), 4.56 min (1*R*, 2*R*); HRMS (M+Na) calcd. for $C_{15}H_{20}O_3S$: 303.3716, found: 303.3712.

***trans*-(±)-2-(Naphthalen-3-ylthio)cyclohexyl acetate (9a)**: Yield: 73%; $^1$H NMR ($CDCl_3$, 300 MHz), $\delta$ [ppm]: 1.27–1.39 (m, 4H), 1.72–1.73 (m, 2H), 2.12–2.16 (m, 2H), 2.89–2.94 (m, 2H), 3.43 (m, 1H), 7.18–7.54 (m, 5H); $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ [ppm]: 22.1, 25.2, 28.2, 33.8, 58.9, 74.6, 127.3, 128.1, 128.9, 129.9, 130.2, 133.0, 134.2, 170.2; HPLC analysis: Yield: 46%; Daicel chiralpak OD-H, hexane/i-PrOH 97/3, 1.0 mL/min, 220 nm, retention times: 4.68 min

(1*S*, 2*S*), 5.38 min (1*R*, 2*R*); HRMS (M+Na) calcd. for $C_{18}H_{20}O_2S$: 323.1179, found: 323.1184.

***trans*-(±)-2-(Cyclohexylthio)cyclohexyl acetate (10a)**: Yield: 78%; $^1$H NMR ($CDCl_3$, 300 MHz), $\delta$ [ppm]: 1.39–1.49 (m, 10H), 1.52–1.90 (m, 8H), 2.02–2.48 (m,4H), 3.07 (m, 1H), 4.18 (m, 1H); $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ [ppm]: 21.0, 21.6, 24.2, 24.4, 24.7, 27.6, 29.9, 34.9, 47.7, 75.3, 170.3. HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 0.5 mL/min, 220 nm, retention times: 4.20 min (1*S*, 2*S*), 5.14 min (1*R*, 2*R*).

***trans*-(±)-2-(Phenylthio)cyclopentyl acetate (11a)**: Yield: 92%; $^1$H NMR ($CDCl_3$, 300 MHz), $\delta$ [ppm]: 1.46–1.94 (m, 6H), 2.03 (s, 3H), 3.10–3.14 (m, 1H), 4.11–4.26 (m, 1H), 7.02–7.22 (m, 5H); $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$ [ppm]: 21.2, 28.0, 30.4, 44.7, 76.1, 126.6, 129.5, 136.3, 170.2; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95:5, 0.5 mL/min, 220 nm, retention times: 4.72 min (1*S*, 2*S*), 5.73 min (1*R*, 2*R*); HRMS (M+Na) calcd. for $C_{13}H_{16}O_2S$: 259.0765, found: 259.0799.

**(±)-1-(Phenylthio)butan-2-yl acetate (12a)**: Yield: 83%;$^1$H NMR ($CDCl_3$, 300 MHz), $\delta$ [ppm]: 0.90–0.92 (m, 3H), 1.63–1.96 (m, 5H), 3.01–3.16 (s, 2H), 4.94–4.96 (m, 1H), 7.18–7.40 (m, 5H); HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95:5, 0.5 mL/min, 220 nm, retention times: 5.63 min (*S*), 6.27 min (*R*).

***trans*-(±)-3-(Phenylthio)butan-2-yl acetate (13a)**: Yield: 71%; $^1$H NMR ($CDCl_3$, 300 MHz), $\delta$ [ppm]: 0.94–0.99 (m, 2H), 1.49–1.61 (m, 3H), 2.80–2.88 (m, 1H), 3.12–3.18 (m, 1H), 3.56–3.64 (m, 1H), 7.18–7.39 (m, 5H); HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95:5, 0.5 mL/min, 220 nm, retention times: 5.02 min (1*S*, 2*S*), 5.81 min (1*R*, 2*R*).

### *4.4. General procedure for resolution of racemic aryl β-hydroxy sulfides*

A solution of the (±)-1 (100 mg) and vinyl acetate (4.5 ml, 50 mmol) was stirred with Immobilized *C. antartica* B (100 mg, 1 eq. w/w) at 27 °C. The reaction was monitored by taking out aliquots at regular intervals and analyzed with HPLC. The reaction was stopped by filtering the enzyme on a sintered glass funnel. Concentration of the filtrate followed by column chromatography provided (1*R*, 2*R*)-**1a-13a** and (1*S*, 2*S*)-**1-13**.

**(1*S*, 2*S*)-2-(Phenylthio)cyclohexanol (1)**: Yield: 46%, $[\alpha]_D^{25}$ = +62.4° (c 1.00, $CHCl_3$); >99% ee; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 0.5 mL/min, 220 nm, retention time: 21.66 (1*S*, 2*S*) min.

**(1*R*, 2*R*)-2-(Phenylthio)cyclohexyl acetate (1a)**: Yield: 42%, $[\alpha]_D^{25}$ = +19.6° (c 0.50, $CHCl_3$); 99% ee; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 0.5 mL/min, 220 nm, retention time: 11.23 min (1*R*, 2*R*).

**(1*S*, 2*S*)-2-(*p*-Tolylthio)cyclohexanol (2)**: Yield: 43%; $[\alpha]_D^{25}$ = +65.8° (c 1.00, $CHCl_3$); >99% ee; HPLC analysis: Daicel Chiralcel OD-H, hexane/i-PrOH = 9/1, flow rate = 0.5 mL/min, 220 nm, retention time: 18.72 min (1*S*, 2*S*).

**(1*R*, 2*R*)-2-(*p*-Tolylthio)cyclohexyl acetate (2a)**: Yield: 45%; $[\alpha]_D^{25}$ = +16.7° (c 1.00, $CHCl_3$); 99% ee; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 0.5 mL/min, 220 nm, retention time: 6.63 min (1*R*, 2*R*).

**(1*S*, 2*S*)-2-(4-Chlorophenylthio)cyclohexanol (3)**: Yield: 37%; $[\alpha]_D^{25}$ = +67.1° (c 1.00, $CHCl_3$); >99% ee; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 1.0 mL/min, 220 nm, retention times: 13.26 min (1*S*, 2*S*).

**(1*R*, 2*R*)-2-(4-Chlorophenylthio)cyclohexyl acetate (3a)**: Yield: 47%; $[\alpha]_D^{25}$ = +24.3° (c 1.00, $CHCl_3$); 99% ee; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 1.0 mL/min, 220 nm, retention times: 5.78 min (1*R*, 2*R*).

**(1*S*, 2*S*)-2-(3-Chlorophenylthio)cyclohexanol (4)**: Yield: 37%; $[\alpha]_D^{25}$ = +67.1° (c 1.00, $CHCl_3$); >99% ee; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 1.0 mL/min, 220 nm, retention time: 11.55 min (1*S*, 2*S*).

**(1*R*, 2*R*)-2-(3-Chlorophenylthio)cyclohexyl acetate (4a)**: Yield 42%; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 1.0 mL/min, 220 nm, retention time: 5.14 min (1*R*, 2*R*).

**(1*S*, 2*S*)-2-(2-Chlorophenylthio)cyclohexanol (5)**: Yield: 42%; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 1.0 mL/min, 220 nm, retention time: 12.40 min (1*S*, 2*S*).

**(1*R*, 2*R*)-2-(2-Chlorophenylthio)cyclohexyl acetate (5a)**: Yield: 47%; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95:5, 1.0 mL/min, 220 nm, retention time: 4.36 min (1*R*, 2*R*).

**(1*S*, 2*S*)-2-(4-Bromophenylthio)cyclohexanol (6)**: Yield: 41%; $[\alpha]_D^{25}$ = +50.6° (c 1.00, $CHCl_3$); 99% ee; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 0.3 mL/min, 220 nm, retention times: 20.33 min (1*S*, 2*S*).

**(1*R*, 2*R*)-2-(4-Bromophenylthio)cyclohexyl acetate (6a)**: Yield: 35%; $[\alpha]_D^{25}$ = +28.6° (c 1.00, $CHCl_3$); 99% ee; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95:5, 0.3 mL/min, 220 nm, retention time: 6.41 min (1*R*, 2*R*).

**(1*S*, 2*S*)-2-(4-Fluorophenylthio)cyclohexanol (7)**: Yield: 41%; $[\alpha]_D^{25}$ = +48.7° (c 1.00, $CHCl_3$); 99% ee; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 0.5 mL/min, 254 nm, retention times: 17.20 min (1*S*, 2*S*).

**(1*R*, 2*R*)-2-(4-Fluorophenylthio)cyclohexyl acetate (7a)**: Yield: 44%; $[\alpha]_D^{25}$ = +6.8° (c 1.00, $CHCl_3$); 99% ee; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95:5, 0.5 mL/min, 254 nm, retention time: 11.50 min (1*R*, 2*R*).

**(1*S*, 2*S*)-2-(4-Methoxyphenylthio)cyclohexanol (8)**: Yield = 42%; $[\alpha]_D^{25}$ = +56.2° (c 1.00, $CHCl_3$); 99% ee; HPLC analysis: Daicel Chiralcel OD-H, hexane/i-PrOH = 9/1, flow rate = 0.5 mL/min, 220 nm, retention time: 17.82 min (1*S*, 2*S*).

**(1*R*, 2*R*)-2-(4-Methoxyphenylthio)cyclohexyl acetate (8a)**: Yield = 47%; $[\alpha]_D^{25}$ = +7.4° (c 1.00, $CHCl_3$); 99% ee; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 97/3, 1.0 mL/min, 220 nm, retention times: 4.56 min (1*R*, 2*R*).

**(1*S*, 2*S*)-2-(Naphthalen-3-ylthio)cyclohexanol (9)**: Yield: 40%; $[\alpha]_D^{25}$ = +53.1° (c 1.00, $CHCl_3$); 99% ee; HPLC analysis: Daicel chiralpak AS-H, hexane/i-PrOH 97/3, 1.0 mL/min, 220 nm, retention time: 11.04 min (1*S*, 2*S*).

**(1*R*, 2*R*)-2-(Naphthalen-3-ylthio)cyclohexyl acetate (9a)**: HPLC analysis: Yield: 46%; Daicel chiralpak OD-H, hexane/i-PrOH 97/3, 1.0 mL/min, 220 nm, retention times: 5.38 min (1*R*, 2*R*).

**(1*S*, 2*S*)-2-(Cyclohexylthio)cyclohexanol (10)**: Yield: 35%; $[\alpha]_D^{25}$ = +44.3° (c 1.00, $CHCl_3$); 99% ee; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 0.5 mL/min, 220 nm, retention time: 19.93 min (1*S*, 2*S*).

**(1*R*, 2*R*)-2-(Cyclohexylthio)cyclohexyl acetate (10a)**: Yield: 38%; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 0.5 mL/min, 220 nm, retention times: 5.14 min (1*R*, 2*R*).

**(1*S*, 2*S*)-2-(Phenylthio)cyclopentanol (11)**: Yield: 45%; $[\alpha]_D^{25}$ = +23.2° (c 1.00, $CHCl_3$); 99% ee; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 90/10, 0.5 mL/min, 220 nm, retention time: 12.51 min (1*S*, 2*S*).

**(1*R*, 2*R*)-2-(Phenylthio)cyclopentyl acetate (11a)**: Yield: 43%; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95:5, 0.5 mL/min, 220 nm, retention times: 5.73 min (1*R*, 2*R*).

**(1*S*, 2*S*)-1-(Phenylthio)butan-2-ol (12)**: Yield: 44%; $[\alpha]_D^{25}$ = +62.6° (c 1.00, $CHCl_3$); 99% ee; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95/5, 0.5 mL/min, 220 nm, retention times: 10.93 min (*S*).

**(*R*)-1-(Phenylthio)butan-2-yl acetate (12a)**: Yield: 40%; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95:5, 0.5 mL/min, 220 nm, retention times: 6.27 min (*R*).

**(1*S*, 2*S*)-3-(Phenylthio)butan-2-ol (13)**: Yield: 46%; $[\alpha]_D^{25}$ = +36.7° (c 1.00, $CHCl_3$); 99% ee; HPLC analysis: Daicel

chiralpak OD-H, hexane/i-PrOH 95/5, 0.5 mL/min, 220 nm, retention times: 11.80 min (1*S*, 2*S*).

**(1*R*, 2*R*)-3-(Phenylthio)butan-2-yl acetate (13a)**: Yield: 41%; HPLC analysis: Daicel chiralpak OD-H, hexane/i-PrOH 95:5, 0.5 mL/min, 220 nm, retention times: 5.81 min (1*R*, 2*R*).

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