Enantiocomplementary Resolution of 2-Phenylthio-2-cyclopentenol and 2-Phenylthio-2-cyclohexenol Using the Same Lipase

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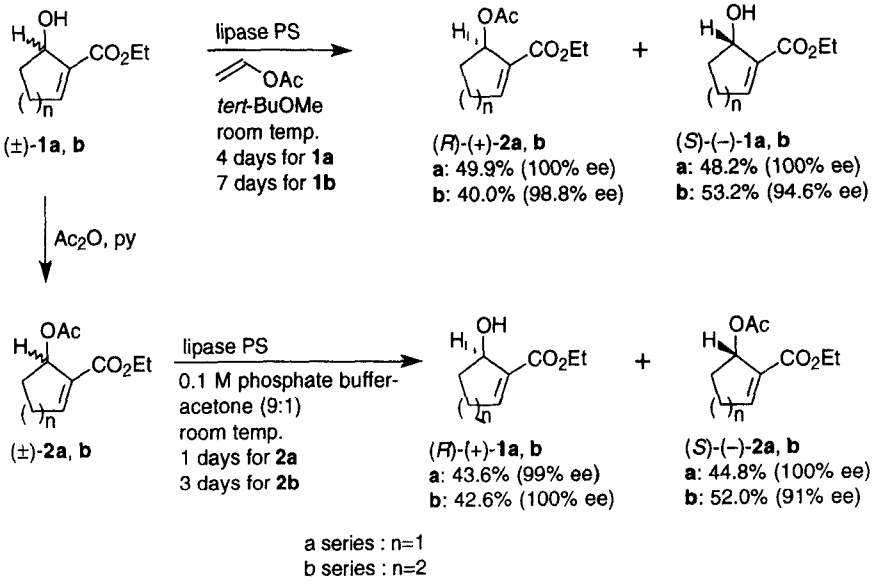
Both racemic 2-phenylthio-2-cyclopentenol (±)-**(3a)** and 2-phenylthio-2-cyclohexenol (±)-**(3b)** afford the corresponding (*R*)-acetates (*R*)-**4a,b** and the unreacted (*S*)-alcohols (*S*)-**3a,b**, respectively, in excellent optical and chemical yields on treatment with vinyl acetate in the presence of lipase PS in dichloromethane. On the other hand, both racemic acetates (±)-**4a,b** obtained from racemic 2-phenylthio-2-cyclopentenol (±)-**(3a)** and 2-phenylthio-2-cyclohexenol (±)-**(3b)** afford the corresponding (*R*)-alcohols (*R*)-**3a,b** and the unreacted (*S*)-acetates (*S*)-**4a,b**, respectively, in excellent optical and chemical yields on stirring in a phosphate buffer–acetone solution in the presence of the same lipase.

Despite their simple structures, it is practically not easy to obtain 2-cyclopentenol and 2-cyclohexenol in optically pure forms.[1] However, because of their high potential as basic chiral building blocks, development of efficient practical preparations of these compounds as well as their synthetic equivalents would be a considerable advantage to the synthesis of a wide variety of optically active compounds. We report an efficient enzymatic method for the enantiocomplementary resolution of 2-phenylthio derivatives of cyclic allylic alcohols which serve as potential synthetic equivalents of optically active 2-cyclopentenol and 2-cyclohexenol.

The direct enzymatic resolution of 2-cyclopentenol and 2-cyclohexenol reported previously[2] showed unsatisfactory enantioselectivity, and we, therefore, used their 2-phenylthio derivatives, **3** and **4**, as synthetic equivalents.[3] We have found that both 2-ethoxycarbonyl derivatives[4] of 2-cyclopentenol (±)-**1a** and 2-cyclohexenol (±)-**1b** as well as their acetates (±)-**2a,b** are resolved excellently with satisfactory chemical yields in the presence of lipase PS (*Pseudomonas* sp. Amano) in an enantiocomplementary manner.[5,6] The former afforded (*R*)-acetates (*R*)-**2a,b** leaving (*S*)-alcohols (*S*)-**1a,b** on exposure to vinyl acetate in *tert*-butyl methyl ether, while the latter afforded the enantiomeric (*R*)-alcohols (*R*)-**1a,b** leaving enantiomeric (*S*)-acetates (*S*)-**2a,b** under hydrolytic conditions in a phosphate buffer solution, both in the presence of lipase PS (Scheme 1). Since the observed high enantioselectivity was apparently due to the bulkiness of the 2-substituent, we used substrates bearing a 2-phenylthio functionality, being an appropriate size to increase the enantioselectivity and easily removed.

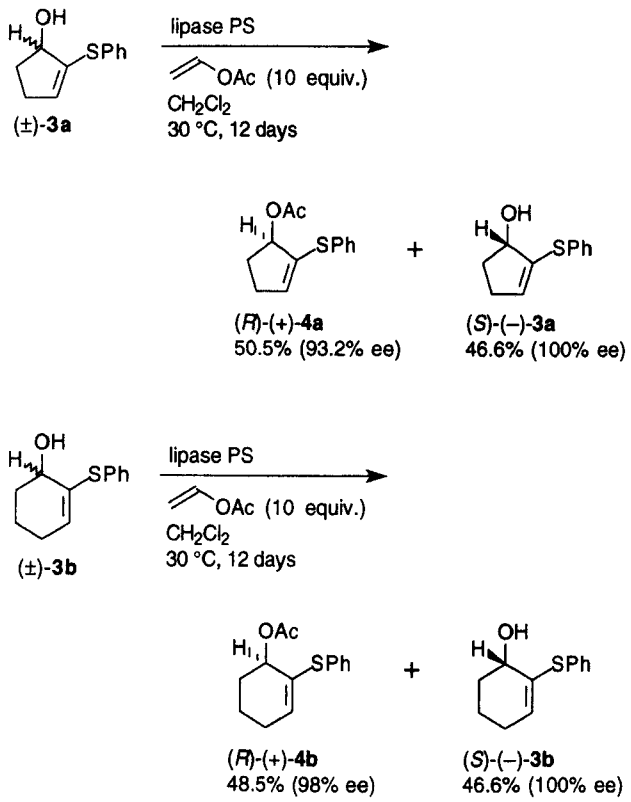
The hydroxy substrates (±)-**3a,b** were prepared in satisfactory yields from known α,β-unsaturated ketones[9,10] by chemoselective 1,2-reduction[7,8] and the acetoxy substrates (±)-**4a,b** were prepared from (±)-**3a,b** by a standard procedure.

We first examined the resolution of the racemic alcohols (±)-**3a,b** under transesterification conditions using vinyl acetate in an organic solvent in the presence of lipase PS. Of the three organic solvents examined (*tert*-butyl methyl ether, toluene, and dichloromethane), dichloromethane showed the best results though the reaction time was somewhat longer. Thus, the racemic alcohols (±)-**3a,b** were stirred with lipase PS (100 mg/mmol of substrate) in dichloromethane (5 mL/mmol of substrate) at 30 °C. The reactions proceeded slowly and were terminated after 12 days to give a 1:1 mixture of the acetates (*R*)-**4a,b** and the unchanged starting materials (*S*)-**3a,b** which were readily separable by silica gel chromatography. A satisfactory level of chemical and optical yields were obtained in both cases. Optical purities of the acetates **4a,b** and the unreacted alcohols **3a,b** were readily determined



Scheme 1

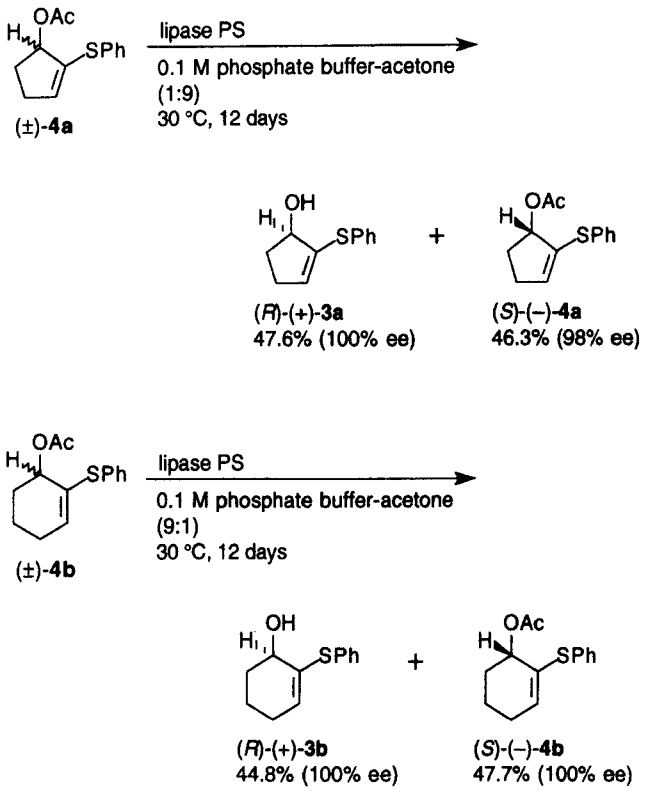
by HPLC using a chiral column. The stereochemical outcome, which was concluded spectroscopically was also in agreement with that observed in the reaction of the 2-carbethoxy-[5] and the 2-(2-trimethylsilylethynyl)-[6c] analogs using the same lipase (Scheme 2).



Scheme 2

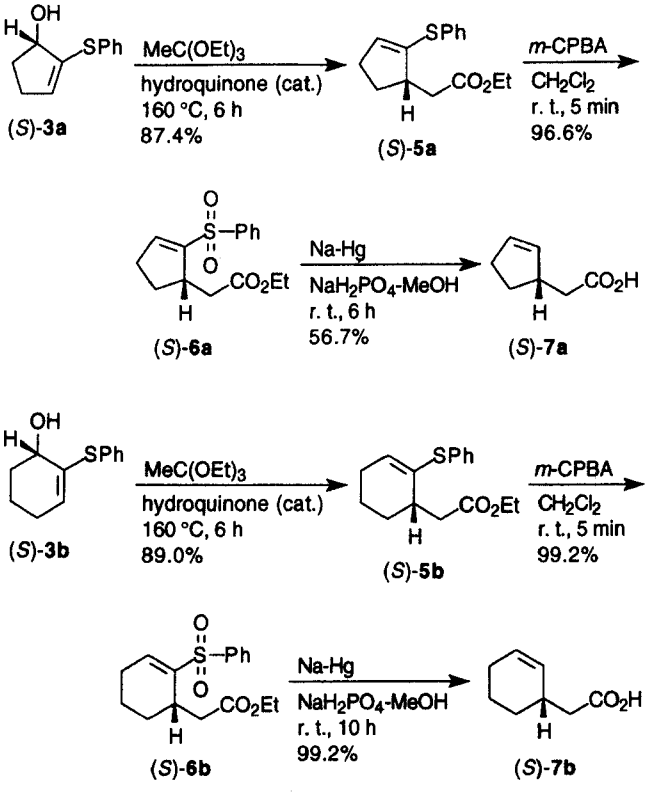
Having obtained satisfactory results in the resolution of racemic alcohols (±)-**3a,b** under transesterification conditions, we next examined the resolution of racemic acetates (±)-**4a,b** under hydrolytic conditions using mixtures of phosphate buffer and acetone in the presence of the same lipase. Although the reaction rate of the two substrates was considerably dependent on the buffer–acetone ratio, we found optimal conditions for an excellent resolution of each compound. Thus, stirring the racemic cyclopentenyl acetate (±)-**4a** with lipase PS (100 mg/mmol of substrate) in a 1:9 mixture of 0.1 M phosphate buffer and acetone (5 mL/mmol of substrate) at 30 °C furnished the optically pure (*R*)-alcohol (*R*)-**3a** in 47.6% yield leaving the optically enriched (98% ee) (*S*)-acetate (*S*)-**4a** in 46.3% yield after 12 days. Similarly, stirring the racemic cyclohexenyl acetate (±)-**4b** with lipase PS in a 9:1 mixture of 0.1 M phosphate buffer and acetone at 30 °C furnished the optically pure (*R*)-alcohol (*R*)-**3b** in 44.8% yield leaving the optically pure (*S*)-acetate (*S*)-**4b** in 47.7% yield after 12 days. Again optical purities of the products were determined by HPLC using a chiral column (Scheme 3).

The configuration of the products obtained was deduced by ^{1}H NMR analysis of the MTPA esters of (*R*)- and (*S*)-**3a,b** by correlation with the empirical rule[11] as well



Scheme 3

as by a chemical correlation by transforming them into the known γ,δ-unsaturated carboxylic acids (*S*)-**7a**,[12] **b**[13] via the sulfide esters (*S*)-**5a,b** and the sulfones (*S*)-**6a,b** by sequential Johnson–Claisen rearrangement,[14] peracid oxidation, and amalgam reduction[15] (Scheme 4).



Scheme 4

In conclusion, we have established an efficient enantiocomplementary synthesis of both enantiomeric 2-phenylthio-2-cyclohexenol (*R*)- and (*S*)-**3a,b** and their acetates (*R*)- and (*S*)-**4a,b**, by using the same lipase. Although it may be characteristic of enzyme reactions, the observed clear-cut resolution leading to enantiocomplementary production of both enantiomeric pairs of the alcohols (*R*)- and (*S*)-**3a,b** and their acetates (*R*)- and (*S*)-**4a,b** by the same lipase is particularly noteworthy.

These compounds may be used not only as synthetic equivalents of optically active 2-cyclopentenol and 2-cyclohexenol, but also as more versatile chiral synthons by utilizing the 2-phenylthio functionality as a handle for various chemical transformations.

IR spectra were recorded on a JASCO-IR-700 spectrometer. ^{1}H NMR spectra were recorded on a Hitachi R-300 spectrometer (300 MHz). Mass spectra were measured on a JEOL JMS-DX303 instrument. Optical rotations were measured with a JASCO-DIP-370 digital polarimeter. Optical purities were determined on a Gilson Model-307 instrument equipped with a chiral column. Satisfactory microanalyses obtained for all compounds: C ± 0.08, H ± 0.16, S ± 0.22.

(±)-2-Phenylthio-2-cyclopentenol [(±)-3a]:
To a stirred suspension of 2-phenylthiocyclopentenone (2.72 g, 14.3 mmol) and $CeCl_3 \cdot 7H_2O$ (5.85 g, 15.7 mmol) in MeOH (70 mL) was added $NaBH_4$ (544.0 mg, 14.3 mmol) portionwise at 0 °C and the mixture stirred at this temperature for 1 h. The reaction was quenched by addition of an appropriate amount of acetone and the mixture evaporated under reduced pressure to remove most of the volatile material. The residue was diluted with H_2O and extracted with Et_2O. The extract was washed with brine, dried ($MgSO_4$), evaporated under reduced pressure, and chromatographed on silica gel (80 g, 20% v/v Et_2O–hexane) to give the cyclopentenol (±)-**3a** as a pale yellow oil; yield: 2.61 g (94.9%).

IR (neat): ν = 3500–3100, 1582 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.84–2.03 (2 H, m, 1 H exchangeable with D_2O), 2.25–2.43 (2 H, m), 2.46–2.61 (1 H, m), 4.68 (1 H, t, J = 3.3, 2.9 Hz), 5.92 (1 H, t, J = 2.6, 1.8 Hz), 7.21–7.35 (3 H, m), 7.37–7.44 (2 H, m).

MS: m/z = 192 (M^+, 100%).

HRMS: Calc. for $C_{11}H_{12}OS$: 192.0609. Found: 192.0623.

(±)-2-Phenylthio-2-cyclohexenol; [(±)-3b]:
To a stirred suspension of the 2-phenylthiocyclohexenone (3.63 g, 17.8 mmol) and $CeCl_3 \cdot 7H_2O$ (7.27 g, 19.5 mmol) in MeOH (90 mL) was added $NaBH_4$ (679.1 mg, 17.8 mmol) portionwise at 0 °C and the mixture stirred at this temperature for 1 h. The reaction was quenched by addition of an appropriate amount of acetone and the mixture evaporated under reduced pressure to remove most of the volatile material. The residue was diluted with H_2O and extracted with Et_2O. The extract was washed with brine, dried ($MgSO_4$), evaporated under reduced pressure, and chromatographed on silica gel (110 g, 15% v/v Et_2O–hexane) to give the cyclohexenol (±)-**3b** as a pale yellow oil; yield: 3.47 g (94.6%).

IR (neat): ν = 3600–3100, 1581 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.50–2.00 (4 H, m), 2.15–2.30 (2 H, m), 2.28 (1 H, bs, exchangeable with D_2O), 4.05 (1 H, bs), 6.26 (1 H, t, J = 4.0, 3.7 Hz), 7.20–7.40 (5 H, m).

MS: m/z = 206 (M^+), 110 (100%).

HRMS: Calc. for $C_{12}H_{14}OS$: 206.0766. Found: 206.0744.

(±)-1-Acetoxy-2-phenylthio-2-cyclopentene; [(±)-4a]:
A mixture of the cyclopentenol (±)-**3a** (889.8 mg, 4.63 mmol), Ac_2O (1.31 mL, 13.9 mmol), Et_3N (1.93 mL, 13.9 mmol), and 4-*N*,*N*-dimethylaminopyridine (16.9 mg, 0.14 mmol) in CH_2Cl_2 (23 mL) was stirred at r. t. for 12 h. The mixture was treated with aq 5% $NaHCO_3$ and extracted with CH_2Cl_2. The extract was washed with brine, dried ($MgSO_4$), evaporated under reduced pressure and chromatographed on silica gel (30 g, 10% v/v Et_2O–hexane) to give the cyclopentenyl acetate (±)-**4a** as a colorless oil; yield: 1.018 g (93.8%).

IR (neat): ν = 1735, 1581 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.96 (3 H, s), 1.83–2.00 (1 H, m), 2.30–2.44 (2 H, m), 2.44–2.62 (1 H, m), 5.66 (1 H, t, J = 4.7, 2.6 Hz), 5.94 (1 H, br s), 7.23–7.37 (3 H, m), 7.38–7.48 (2 H, m).

MS: m/z = 234 (M^+), 174 (100%).

HRMS: Calc. for $C_{13}H_{14}O_2S$: 234.0715. Found: 234.0715.

(±)-1-Acetoxy-2-phenylthio-2-cyclohexene; [(±)-4b]:
A mixture of the cyclohexenol (±)-**3b** (918.6 mg, 4.45 mmol), Ac_2O (1.25 mL, 13.3 mmol), Et_3N (1.85 mL, 13.3 mmol), and 4-*N*,*N*-dimethylaminopyridine (16.2 mg, 0.13 mmol) in CH_2Cl_2 (22 mL was stirred at r. t. for 12 h. The mixture was treated with aq 5% $NaHCO_3$ and extracted with CH_2Cl_2. The extract was washed with brine, dried ($MgSO_4$), evaporated under reduced pressure and chromatographed on silica gel (30 g, 10% v/v Et_2O–hexane) to give the cyclohexenyl acetate (±)-**4b** as a colorless oil; yield: 1.08 g.

IR (neat): ν = 1731, 1581 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.60–1.90 (4 H, m), 1.93 (3 H, s), 2.10–2.40 (2 H, m), 5.29 (1 H, bs), 6.34 (1 H, dd, J = 4.6, 3.7 Hz), 7.20–7.40 (5 H, m).

MS: m/z = 248 (M^+), 188 (100%).

HRMS: Calc. for $C_{14}H_{16}O_2S$: 248.0871. Found: 248.0858.

Lipase-Mediated Transesterification of the Racemic Cyclopentenol (±)-3a:
A suspension of (±)-**3a** (1.04 g, 5.41 mmol), vinyl acetate (5.0 mL, 54.4 mmol), and lipase PS (Amano, *Pseudomonas* sp., 541 mg) in CH_2Cl_2 (27 mL) was stirred at 30 °C for 12 d. The reaction mixture, after being filtered through a Celite pad, was evaporated under reduced pressure and chromatographed on silica gel (50 g, 10 ~ 20% v/v Et_2O–hexane) to give the (*R*)-acetate (*R*)-**4a** as a colorless oil; yield: 640 mg (50.5%), $[\alpha]_D^{29}$ = + 80.0° (c = 1.28, $CHCl_3$), and (*S*)-alcohol (*S*)-**3a** as a colorless oil; yield: 485 mg (46.6%), $[\alpha]_D^{32}$ = − 153.8° (c = 1.02, $CHCl_3$).

The optical purity of (*R*)-**4a** was determined to be 93.2% ee by HPLC (Chiralcel OD, 1% v/v *i*-PrOH–hexane). Spectroscopic data and TLC were identical with those of (±)-**4a**.

The optical purity of (*S*)-**3a** was determined to be 100% ee by HPLC (Chiralcel OD, 5% v/v *i*-PrOH–hexane). Spectroscopic data and TLC were identical with those of (±)-**3a**.

Lipase-Mediated Transesterification of the Racemic Cyclohexenol (±)-3b:
A suspension of (±)-**3b** (1.02 g, 4.95 mmol), vinyl acetate (4.58 mL, 49.7 mmol), and lipase PS (Amano, *Pseudomonas* sp., 495 mg) in CH_2Cl_2 (25 mL) was stirred at 30 °C for 12 d. The reaction mixture, after being filtered through a Celite pad, was evaporated under reduced pressure and chromatographed on silica gel (50 g, 5 ~ 15% v/v Et_2O–hexane) to give the (*R*)-acetate (*R*)-**4b** as a colorless oil; yield: 596 mg (48.5%), $[\alpha]_D^{31}$ = + 191.2° (c = 1.29, $CHCl_3$), and (*S*)-alcohol (*S*)-**3b** as a colorless oil; yield: 476 mg (46.6%), $[\alpha]_D^{31}$ = − 283.3° (c = 1.29, $CHCl_3$).

The optical purity of (*R*)-**4b** was determined to be 98.0% ee by HPLC (Chiralcel OD, 1% v/v *i*-PrOH–hexane). Spectroscopic data and TLC were identical with those of (±)-**4b**.

The optical purity of (*S*)-**3b** was determined to be 100% ee by HPLC (Chiralcel OD, 5% v/v *i*-PrOH–hexane). Spectroscopic data and TLC were identical with those of (±)-**3b**.

Lipase-mediated Hydrolysis of the Racemic Cyclopentenyl Acetate [(±)-4a]:
A suspension of (±)-**4a** (965 mg, 4.12 mmol) and lipase PS (Amano, *Pseudomonas* sp., 412 mg) in a mixture of 0.1 M phosphate buffer and acetone (1:9 v/v, 20 mL) was stirred at 30 °C for 12 d. The reaction mixture, after being filtered through a Celite pad, was evaporated under reduced pressure and chromatographed on silica gel (50 g, 10 ~ 20% v/v Et_2O-hexane) to give the (*S*)-acetate (*S*)-**4a**

as a colorless oil; yield: 447 mg (46.3%), $[\alpha]_D^{30} = -84.0°$ ($c = 1.12$, $CHCl_3$), and (*R*)-alcohol (*R*)-**3a** as a colorless oil; yield: 377 mg (47.6%), $[\alpha]_D^{32} = +154.1°$ ($c = 1.10$, $CHCl_3$).

The optical purity of (*S*)-**4a** was determined to be 98% ee by HPLC (Chiralcel OD 1% v/v *i*-PrOH–hexane). Spectroscopic data and TLC were identical with those of (±)-**4a**.

The optical purity of (*R*)-**3a** was determined to be 100% ee by HPLC (Chiralcel OD, 5% v/v *i*-PrOH–hexane). Spectroscopic data and TLC were identical with those of (±)-**3a**.

Lipase-Mediated Hydrolysis of the Racemic Cyclohexenyl Acetate [(±)-4b]:

A suspension of (±)-**4b** (103 mg, 0.415 mmol) and lipase PS (Amano, *Pseudomonas* sp., 41.5 mg) in a mixture of 0.1 M phosphate buffer and acetone (9:1 v/v, 2 mL) was stirred at 30°C for 12 d. The reaction mixture, after being filtered through a Celite pad, was evaporated under reduced pressure and chromatographed on silica gel (5 g, 5 ~ 15% v/v Et_2O–hexane) to give the (*S*)-acetate (*S*)-**4b** as a colorless oil; yield: 49.2 mg (47.7 mg), $[\alpha]_D^{28} = -194.8°$ ($c = 0.47$, $CHCl_3$), and (*R*)-alcohol (*R*)-**3b** as a colorless oil; yield: 38.4 mg (44.8%), $[\alpha]_D^{31} = +277.6°$ ($c = 1.32$, $CHCl_3$).

The optical purity of (*S*)-**4b** was determined to be 100% ee by HPLC (Chiralcel OD, 1% v/v *i*-PrOH–hexane). Spectroscopic data and TLC were identical with those of (±)-**4b**.

The optical purity of (*R*)-**3b** was determined to be 100% ee by HPLC (Chiralcel OD, 5% v/v *i*-PrOH–hexane). Spectroscopic data and TLC were identical with those of (±)-**3b**.

Ethyl (*S*)-2-Phenylthio-2-cyclopentene-1-acetate; [(*S*)-5a]:

A solution of (*S*)-**3a** (295.3 mg, 1.53 mmol) and hydroquinone (16.8 mg, 0.15 mmol) in triethyl orthoacetate (1.41 mL, 7.69 mmol) was heated at 160°C for 10 h with removal of low boiling material using a Dean–Stark apparatus. After evaporation of any excess triethyl orthoacetate under reduced pressure, the residue was chromatographed on silica gel (30 g, 3% v/v Et_2O–hexane) to give the (*S*)-ester (*S*)-**5a** as a colorless oil; yield: 352 mg (87.4%), $[\alpha]_D^{27} = +52.7°$ ($c = 1.08$, $CHCl_3$).

IR (neat): $\nu = 1735$, 1582 cm^{-1}.

^1H NMR ($CDCl_3$): $\delta = 1.22$ (3 H, t, $J = 6.9$ Hz), 1.65–1.80 (1 H, m), 2.17 (1 H, dd, $J = 15.4$, 10.2 Hz), 2.19–2.32 (2 H, m), 2.34–2.44 (2 H, m), 2.71 (1 H, dd, $J = 15.5$, 4.0 Hz), 3.03–3.18 (1 H, m), 4.09 (2 H, q, $J = 6.9$ Hz), 5.78 (1 H, dd, $J = 4.0$, 2.2 Hz), 7.18–7.40 (5 H, m).

MS: $m/z = 262$ (M^+), 153 (100%).

HRMS: Calc. for $C_{15}H_{18}O_2S$: 262.1028. Found: 262.1071.

Ethyl (*S*)-2-Phenylthio-2-cyclohexene-1-acetate; [(*S*)-5b]:

A solution of (*S*)-**3b** (1.07 g, 5.23 mmol) and hydroquinone (57.5 mg, 0.523 mmol) in triethyl orthoacetate (9.59 mL, 52.3 mmol) was heated at 160°C for 12 h with removal of low boiling material using a Dean–Stark apparatus. After evaporation of any excess triethyl orthoacetate under reduced pressure, the residue was chromatographed on silica gel (50 g, 3% v/v Et_2O–hexane) to give the (*S*)-ester (*S*)-**5b** as a colorless oil; yield: 1.28 g (89.0%), $[\alpha]_D^{27} = -133.5°$ ($c = 0.952$, $CHCl_3$).

IR (neat): $\nu = 1732$, 1583 cm^{-1}.

^1H NMR ($CDCl_3$): $\delta = 1.21$ (3 H, t, $J = 6.9$ Hz), 1.55–1.85 (4 H, m), 2.10–2.22 (2 H, m), 2.28 (1 H, dd, $J = 15.7$, 10.6 Hz), 2.60–2.73 (1 H, m), 2.89 (1 H, dd, $J = 15.4$, 3.6 Hz), 4.08 (2 H, q, $J = 6.9$ Hz), 6.17 (1 H, td, $J = 3.8$, 1.1 Hz), 7.13–7.32 (5 H, m).

MS: $m/z = 276$ (M^+), 167 (100%).

HRMS: Calc. for $C_{16}H_{20}O_2S$: 276.1184. Found: 276.1183.

Ethyl (*S*)-2-Phenylsulfonyl-2-cyclopentene-1-acetate; [(*S*)-6a]:

To a stirred solution of **5a** (145.4 mg, 0.554 mmol) in CH_2Cl_2 (2.0 mL) was added *m*-chloroperbenzoic acid (208.8 mg, 1.22 mmol) in CH_2Cl_2 (1.0 mL) at r.t. After 5 min, the solution was washed with aq 5% $Na_2S_2O_3$, 5% $NaHCO_3$, brine, and dried ($MgSO_4$). The solution was evaporated under reduced pressure and the residue chromatographed on silica gel (20 g, 15% v/v EtOAc–hexane) to give the (*S*)-sulfone (*S*)-**6a** as a colorless oil; yield: 157.7 mg (96.6%), $[\alpha]_D^{25} = -29.2°$ ($c = 3.15$, $CHCl_3$).

IR (neat): $\nu = 1735$, 1583 cm^{-1}.

^1H NMR ($CDCl_3$): $\delta = 1.24$ (3 H, t, $J = 7.3$ Hz), 1.79 (1 H, ddd, $J = 17.4$, 8.6, 4.4 Hz), 2.18–2.34 (1 H, m), 2.28 (1 H, dd, $J = 16.3$, 10.6 Hz), 2.38–2.66 (2 H, m), 2.98 (1 H, dd, $J = 16.3$, 3.3 Hz), 3.10–3.30 (1 H, m), 4.11 (2 H, ddd, $J = 14.2$, 7.1, 1.8 Hz), 6.82 (1 H, dd, $J = 4.0$, 2.5 Hz), 7.48–7.68 (3 H, m), 7.84–7.94 (2 H, m).

MS: $m/z = 294$ (M^+), 125 (100%).

HRMS: Calc. for $C_{15}H_{18}O_4S$: 294.0926. Found: 294.0901.

Ethyl (*S*)-2-Phenylsulfonyl-2-cyclohexene-1-acetate; [(*S*)-6b]:

To a stirred solution of **5b** (232.2 mg, 0.842 mmol) in CH_2Cl_2 (2.5 mL) was added *m*-chloroperbenzoic acid (319.2 mg, 1.85 mmol) in CH_2Cl_2 (1.5 mL) at r.t. After 5 min, the solution was washed with aq 5% $Na_2S_2O_3$, 5% $NaHCO_3$, brine, and dried ($MgSO_4$). The solution was evaporated under reduced pressure and the residue chromatographed on silica gel (35 g, 15% v/v EtOAc–hexane) to give the (*S*)-sulfone (*S*)-**6b** as a colorless oil; yield: 257.0 mg (99.2%), $[\alpha]_D^{24} = -62.1°$ ($c = 1.35$, $CHCl_3$).

IR (neat): $\nu = 1729$, 1583 cm^{-1}.

^1H NMR ($CDCl_3$): $\delta = 1.25$ (3 H, t, $J = 7.3$ Hz), 1.32–1.48 (1 H, m), 1.50–1.74 (3 H, m), 2.10–2.45 (2 H, m), 2.32 (1 H, dd, $J = 16.2$, 10.6 Hz), 2.80–2.93 (1 H, m), 3.05 (1 H, ddd, $J = 16.1$, 2.9, 1.1 Hz), 4.12 (2 H, ddd, $J = 14.2$, 7.3, 1.1 Hz), 7.15 (1 H, t, $J = 3.6$ Hz), 7.48–7.66 (3 H, m), 7.80–7.92 (2 H, m).

MS: $m/z = 308$ (M^+), 167 (100%).

HRMS: Calc. for $C_{16}H_{20}O_4S$: 308.1082. Found: 308.1084.

(*S*)-2-Cyclopentene-1-acetic Acid [(*S*)-7a]:

To a stirred solution of **6a** (157.7 mg, 0.536 mmol) in MeOH (10.0 mL) was added $NaH_2PO_4 \cdot 2H_2O$ (334.4 mg, 2.14 mmol) and 5% Na–Hg (806.0 mg) at r.t. and stirring was continued for 6 h at this temperature. Hydrolysis of the ester bond occurred under these conditions. The mixture was filtered through a Celite pad and the filtrate was evaporated under reduced pressure. The residue was diluted with 5% HCl and the solution was extracted with Et_2O. The dried extract ($MgSO_4$) was evaporated under reduced pressure and the residue chromatographed on silica gel (10 g, 30% v/v EtOAc–hexane containing 1% AcOH) to give the known (*S*)-acid (*S*)-**7a** as a pale yellow oil; yield: 38.3 mg, 56.7%), $[\alpha]_D^{24} = +107.4°$ ($c = 0.38$, $CHCl_3$) [lit.[12]: $[\alpha]_D^{30} = +109.2°$ ($c = 5.9$, $CHCl_3$)].

Spectral data (IR and ^1H NMR) were identical with those reported.[16]

IR (neat): $\nu = 3500$–2500, 1709 cm^{-1}.

^1H NMR ($CDCl_3$): $\delta = 1.42$–1.56 (1 H, m), 2.15 (1 H, dtd, $J = 13.0$, 8.2, 5.5 Hz), 2.24–2.50 (4 H, m), 3.02–3.17 (1 H, m), 5.69 (1 H, ddd, $J = 5.8$, 4.0, 1.8 Hz), 5.79 (1 H, ddd, $J = 5.5$, 4.4, 2.2 Hz), 10.20–11.80 (1 H, bs).

MS: $m/z = 126$ (M^+), 67 (100%).

HRMS: Calc. for $C_7H_{10}O_2$: 126.0681. Found: 126.0677.

(*S*)-2-Cyclohexene-1-acetic Acid [(*S*)-7b]:

To a stirred solution of **6b** (285.8 mg, 0.927 mmol) in MeOH (18.0 mg) was added $NaH_2PO_4 \cdot 2H_2O$ (578.4 mg, 3.71 mmol) and 5% Na–Hg (1.393 g) at r.t. and stirring was continued for 10 h at this temperature. The mixture was filtered through a Celite pad and the filtrate evaporated under reduced pressure. The residue was diluted with 5% HCl and the solution extracted with Et_2O. The dried extract ($MgSO_4$) was evaporated under reduced pressure and the residue was chromatographed on silica gel (15 g, 30% v/v EtOAc–hexane containing 1% AcOH) to give the known (*S*)-acid (*S*)-**7b** as a colorless oil; yield: 128.8 mg (99.2%), $[\alpha]_D^{27} = +84.4°$ ($c = 2.57$, $CHCl_3$) [lit.[13]: $[\alpha]_D^{27} = +65°$ ($c = 2.66$, $CHCl_3$), 84% ee].

IR (neat): $\nu = 3500$–2500, 1716 cm^{-1}.

^1H NMR ($CDCl_3$): $\delta = 1.30$ (1 H, dddd, $J = 12.8$, 10.6, 8.2, 2.9 Hz), 1.48–1.64 (1 H, m), 1.65–1.78 (1 H, m), 1.80–1.92 (1 H, m), 1.94–2.04 (2 H, m), 2.34 (2 H, t, $J = 8.4$, 6.6 Hz), 2.60 (1 H, m),

5.56 (1 H, dd, J = 9.9, 1.8 Hz), 5.73 (1 H, ddd, J = 10.1, 5.8, 3.6 Hz), 10.60–12.00 (1 H, bs).

MS: m/z = 140 (M^+), 80 (100%).

HRMS: Calc. for $C_8H_{12}O_2$: 140.0837. Found: 140.0792.

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