Preparation and odour properties of (*S*)-3-mercapto-1-heptyl acetate

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Synthesis of (*S*)-3-mercapto-1-heptyl acetate was achieved in four steps. Sharpless asymmetric epoxidation of (*E*)-2-heptenol yielded (2*R*,3*R*)-2,3-epoxy-1-heptanol, which was treated with thiourea in the presence of $Ti(OPr^i)_4$ to give (2*S*,3*S*)-2,3-epithio-1-heptanol, reduction of which followed by acetylation afforded (*S*)-3-mercapto-1-heptyl acetate in 91% ee. The optically active product possessed a tropical fruit aroma reminiscent of mango and passion fruit, with berry, ester-like, sweet, and pepper-like aspects.

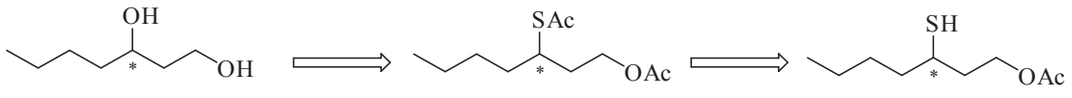
Keywords: (*E*)-2-heptenol, Sharpless asymmetric epoxidation, (2*R*,3*R*)-2,3-epoxy-1-heptanol, (2*S*,3*S*)-2,3-epithio-1-heptanol, chiral flavour

Sulfur-containing compounds are an important family of aroma chemicals due to their low odour thresholds and high impact nature. More and more sulfur-containing aroma chemicals have been identified as volatile components of various foods and plants [1–5] as a result of ongoing interest in discovering new types of flavours. In particular, polyfunctional thiols and their derivatives having pronounced odour qualities have been the subject of many publications.[6–11] A lot of compounds containing 1,3-oxygen–sulfur functionality, such as 3-mercapto-1-hexanol and its derivatives,[12] and 4-mercapto-2-heptanol and its derivatives,[13] have been found to possess tropical, fruity or vegetable odour notes. As a result, the 1,3-oxygen–sulfur functionality has been described as the "olfactophore" for these notes.

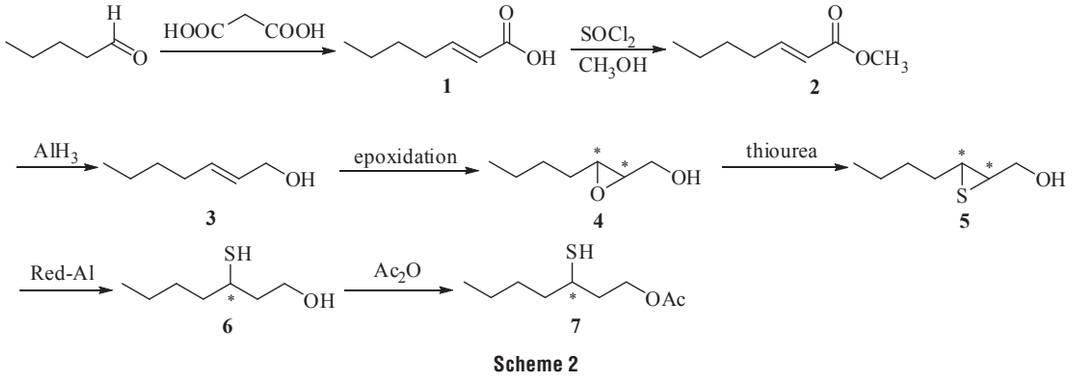
3-Mercaptoheptyl acetate containing the 1,3-oxygen–sulfur olfactophore has been detected in the volatiles of *Ruta chalepensis* L. plant material[14] and approved as a flavour ingredient by the Flavour and Extract Manufacturers' Association (FEMA) in 2007 to appear in the GRAS (Generally Recognised as Safe) list 23 with FEMA No. 4289.[15] It has been reported to be a valuable flavour ingredient, which is distinguished by its highly appreciated and performing bottom notes of tea, citrus-grapefruit and fruity-pear-peach type.[16] Flavouring ingredients capable of imparting well-balanced bottom notes are especially desirable for the flavourists due to their relative rareness. Thus the organoleptic advantages of 3-mercaptoheptyl acetate make it an asset to flavourists. It can be used as the racemate, but the (*S*)-antipode is the more appreciated one. For comparison of the two, both enantiomers have been a target for synthesis.[16]

Escher *et al.*[16] prepared racemic 3-mercaptoheptyl acetate and its enantiomers from the racemic or enantiomerically enriched heptane-1,3-diol, respectively, through a four-step route, including selective acetylation of the primary hydroxy group, nucleophilic substitution of the secondary hydroxy group *via* its sulfonate, reductive removal of acetate and thioacetyl groups of the intermediate, and selective acetylation of the hydroxy group of 3-mercapto-1-heptanol (Scheme 1). Enantiomerically enriched heptane-1,3-diols were obtained by the reduction of methyl (*R*)- or (*S*)-3-hydroxyheptanoate with $LiAlH_4$, respectively. Methyl (*R*)-3-hydroxyheptanoate was prepared in >98% ee according to the method reported by Utaka *et al.*[17] and methyl (*S*)-3-hydroxyhepatanoate was prepared according to the method reported by Oppolzer and Strakemann.[18]

Allyl alcohols have become very versatile substrates since Sharpless first reported their asymmetric epoxidation in 1980.[19] In view of the aforementioned desirable organoleptic properties of (*S*)-3-mercaptoheptyl acetate, we decided to prepare this enantiomer by a simpler four-step approach starting from 2-hepten-1-ol, which is easily accessible by the Knoevenagel condensation of *n*-pentanal with malonic acid (Scheme 2). The odour features of the synthesised product were evaluated by gas chromatography-olfactometry (GC-O) analysis.



Scheme 1



Scheme 2

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Results and discussion

(*E*)-2-Heptenoic acid **1** produced by Knoevenagel condensation of *n*-pentanal with malonic acid was converted to (*E*)-2-hepten-1-ol **3** *via* esterification followed by reduction. The direct reduction of (*E*)-2-heptenoic acid **1** by $LiAlH_4$ gave a mixture of (*E*)-2-hepten-1-ol **3** and heptan-1-ol with poor chemoselectivity, whereas methyl (*E*)-2-heptenoate **2** was reduced by AlH_3 to produce **3** exclusively without the formation of the unwanted saturated alcohol.

In order to obtain reference samples for the determination of ee, the racemate of 3-mercaptoheptyl acetate was prepared first. (*E*)-2-Hepten-1-ol **3** was epoxidised by MCPBA to afford (±)-2,3-epoxy-1-heptanol **4**, treatment of which with thiourea in the presence of Ti $(OPr^i)_4$ and then by saturated aqueous $NaHCO_3$ led to (±)-2,3-epithio-1-heptanol **5** in ~81% yield. Pickenhagen and Brönner–Schindler had shown that treatment of optically active 2,3-epoxy-1-hexanols with thiourea under acidic conditions afforded the corresponding 2,3-epithio-1-hexanols containing 10% by-product of 1,2-epithio-3-hexanol and the desired product was separated from the by-product by preparative GC.[20] In the present work, (±)-1,2-epithio-3-heptanol in (±)-**5** was not detected by ^{1}H NMR analysis, which is consistent with results in the literature.[21] (±)-3-Mercapto-1-heptanol **6** was produced by the reduction of (±)-**5** with Red-Al in THF in about 60% yield. Treatment of (±)-**6** with acetic anhydride in pyridine at –20 °C afforded (±)-3-mercapto-1-heptyl acetate **7** in about 53% yield.

Asymmetric epoxidation of **3** under the Sharpless conditions using D-(–)-diethyl tartrate afforded (2*R*,3*R*)-**4** (94% ee) which was treated with thiourea in the presence of Ti$(OPr^i)_4$ to give (2*S*,3*S*)-**5** (92% ee), a thiirane of inverted absolute configuration. The ee values of both of the epoxides and thiiranes were determined by the resolution of their trifluoroacetate derivatives on a G-TA column of 50 m. The thiirane was obtained from the epoxide with an ee value very close to that of the precursor. The substitution reaction proceeded with high stereoselectivity just as Gao and Sharpless have shown.[21] (2*S*,3*S*)-**5** (92% ee) was reduced with Red-Al to afford (3*S*)-**6** (92% ee), treatment of which with acetic anhydride in pyridine at –20 °C led to (3*S*)-**7** (91% ee). The ee values of optically active **6** and **7** were determined by direct resolution on a G-TA column of 50 m. The results indicated that the reduction of thiirane and acetylation of 3-mercapto-1-heptanol proceeded nearly without any loss of enantiomeric excess. We noticed that the specific rotation value of the intermediate (*S*)-3-mercapto-1-heptanol ($[\alpha]_D^{20} = -1.3^o$ (c 2.65, $CHCl_3$)) was not consistent with that in the literature[16] [$[\alpha]_D^{20} = +4.4^o$ (c 5.0, $CHCl_3$)]. In order to ensure the reliability of the results, a set of parallel experiments were carried out starting from (*E*)-2-hepten-1-ol 3 using L-(+)-diethyl tartrate as a chiral ligand in Sharpless AE. The specific rotation value of the intermediate (*R*)-3-mercapto-1-heptanol obtained from L-(+)-diethyl tartrate was $[\alpha]_D^{20} = +1.3^o$ (c 2.85, $CHCl_3$), which is opposite and equal to that of (*S*)-3-mercapto-1-heptanol obtained from D-(–)-diethyl tartrate. (*R*)-3-Mercapto-1-heptanol was acylated with acetic anhydride to give (*R*)-3-mercaptoheptyl acetate, which gave a very close specific rotation value to that of (R)-enantiomer in the literature.[16]

Compared with the method of Escher *et al*.,[16] our synthetic route is more straightforward, although with a slightly lower ee value. In the synthetic route of Pickenhagen and Brönner–Schindler,[20] (2*R*,3*R*)- or (2*S*,3*S*)-2,3-epithio-1-hexanol was prepared from the Sharpless AE products of (*E*)-2-hexenol by treatment with thiourea in the presence of H_2SO_4. The obtained thiiranes were reduced by Red-Al followed by treatment with NaOH/MeI to lead to (*R*)- and (*S*)-3-methylthio-1-hexanols with an ee of 52 and 78% respectively.[20] Since we avoided acid conditions in our work and observed no racemisation in the reduction of thiiranes, and neither of the last two steps could be responsible, it seems to us very possible that the racemisation occurred owing to the acidic conditions used in their preparation of the thiiranes from the epoxides.

The odour from a smelling strip was described for (±)-**7** as sulfurous, sweet, fruity. The odour properties of (3*S*)-**7** were evaluated by chiral GC-O. (3*S*)-**7** possessed a tropical fruit aroma reminiscent of mango and passion fruit, with berry, ester-like, sweet, and pepper-like aspects.

In summary, the preparation of (±)-3-mercapto-1-heptyl acetate and the (*S*)-enantiomer could be performed in acceptable chemical and/or high optical yields starting from (*E*)-2-heptenol *via* epoxidation, substitution with thiourea, reduction and acetylation. The conversion of epoxide to the corresponding thiirane in the presence Ti$(OPr^i)_4$ avoided the occurrence of racemisation and the formation of certain by-products. The (*S*)-enantiomer offers a unique powerful odour and exhibits good potential as a flavouring ingredient.

Experimental

D-(–) and L-(–)-Diethyl tartrate, Ti $(OPr^i)_4$, t-BuOOH, and sodium bis(2-methoxyethoxy)aluminium hydride (Red-Al) were purchased from Sigma-Aldrich Chemical Co (St. Louis, MO/US). *m*-Chloroperoxybenzoic acid (MCPBA, 70%), and $LiAlH_4$ were purchased from Beijing Bailingwei Science and Technology Company (Beijing, P.R. China). The others were purchased from Beijing Huaxue Shiji Company (Beijing, P.R. China). NMR spectra were obtained on a Bruker AV 300 MHz spectrometer (^{1}H NMR at 300 Hz, ^{13}C NMR at 75 Hz) in $CDCl_3$ using TMS as internal standard. Chemical shifts (δ) are given in ppm and coupling constants (*J*) in Hz. The high resolution mass spectrum was performed on a Bruker Apex IV FTMS. Optical rotations were measured on an Autopol IV digital automatic polarimeter (Rudolph, Hackettstown, NJ, USA).

Chiral GC analysis

An Agilent 6890 GC with a flame ionisation detector (FID) was used for GC analyses (Agilent Technologies, Santa Clara, CA, USA). The column used was a G-TA chiral capillary column (50 m × 0.25 mm × 0.25 μm) from the ASTEC company (Chattanooga, TN, USA). The conditions were as follows: injector temperature 250 °C, detector temperature 250 °C, N_2 as carrier gas, constant flow mode 0.8 mL min^{-1}, split ratio 50/1. The concentration of samples was about 0.5 wt% in dry ether, the injection volume was about 1 μL. The oven temperature was programmed at different rates for different samples. For 2,3-epoxy-1-heptanols **4**, it was from 50 °C to 100 °C at a rate of 10 °C min^{-1}, and held at 100 °C for 1 min; raised to 175 °C at 2 °C min^{-1}, and held at 175 °C for 10 min. For **5**–**7**, it was raised from 50 °C to 100 °C at a rate of 2 °C min^{-1}, and held at 100 °C for 1 min; raised to 150 °C at 1 °C min^{-1}, and held at 150 °C for 8 min; raised to 175 °C at 10 °C min^{-1} and held at 175 °C for 3 min.

Chiral GC-O analysis and evaluation

Chiral GC-O analysis was carried out using an Agilent 6890N gas chromatograph installed with a chiral capillary column G-TA (50 m × 0.25 mm × 0.25 μm), a FID and a sniffing port (Sniffer 9000, Brechbühler Scientific Analytical Solutions INC, Switzerland). The conditions were the same as those in GC analysis. The column effluent was divided (ratio 1 : 1) between the FID detector and the sniffing port through a "Y" shape glass splitter. The effluent from the sniffing port was captured with a stream of humidified air of 16 mL min^{-1} and transferred to the glass detection cone by one length of capillary column at the temperature of 220 °C. Sniffings were carried out by a panel composed of three judges.

(E)-2-Heptenoic acid **1**: A mixture of malonic acid (18 g, 0.2 mol), *n*-pentanal (8.6 g, 0.1 mol) and piperidine (0.5 mL, 5 mmol) in pyridine (50 mL) was stirred at room temperature for 20 h. The mixture was

heated to 45 °C and stirred for 4 h. Then the solution was poured into the mixture of crushed ice and concentrated HCl (50 mL). The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 80 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and then concentrated under reduced pressure. The crude product was distilled under reduced pressure to afford (*E*)-2-heptenoic acid **1** (11 g, 86%) as a pale yellow liquid, b.p. 80–82 °C (1.32 kPa); ^{1}H NMR: δ 0.90 (3 H, t, *J* = 7.2 Hz), 1.26–1.52 (4 H, m), 2.26 (2 H, qd, *J* = 6.9, 1.5 Hz), 5.81 (1 H, td, *J* = 15.6, 1.5 Hz), 7.08 (1 H, td, *J* = 15.6, 6.9 Hz), 12.06 (1H, br); ^{13}C NMR: δ 13.8, 22.2, 29.9, 32.0, 120.6, 152.5, 172.3; GC/MS (EI): *m/z* (%) 41 (73), 55 (39), 68 (60), 73 (100), 86 (31), 99 (54), 110 (18, [M-18]$^+$). The NMR data were consistent with those described in the literature.[22]

Methyl (E)-2-heptenoate **2**: To a solution of (*E*)-2-heptenoic acid **1** (32 g, 0.25 mol) in methanol (120 mL) was added $SOCl_2$ (35.7 g, 0.3 mol) dropwise. The mixture was then heated to reflux for 4 h. Most of the methanol and excess $SOCl_2$ were removed by rotary evaporation. The residue was diluted with water and adjusted pH to 8 by 10% NaOH. The mixture was extracted with CH_2Cl_2 (3 × 80 mL) and the combined organic layers were washed with brine and dried over anhydrous $MgSO_4$. The solution was concentrated by rotary evaporation and the residue was distilled under reduced pressure to afford methyl (*E*)-2-heptenoate **2** (32 g, 90%) as a colourless oil, b.p. 30–32 °C(1.32 kPa); ^{1}H NMR: δ 0.89 (3 H, t, *J* = 7.2 Hz), 1.23–1.50 (4 H, m), 2.19 (2 H, qd, *J* = 6.9, 1.5 Hz), 3.71 (3 H, s), 5.81 (1 H, td, *J* = 15.6, 1.5 Hz), 6.96 (1 H, td, *J* = 15.6, 6.9 Hz); ^{13}C NMR: δ 13.6, 22.0, 30.0, 31.8, 51.2, 120.7, 149.6, 167.0; GC/MS (EI): *m/z* (%) 41 (57), 55 (93), 69 (37), 87 (100), 111 (63), 113 (83), 142 (14, M$^+$). The NMR data were consistent with those described in the literature.[23]

(E)-2-Heptenol **3**: A solution of $LiAlH_4$ (3.75 g, 0.1 mol) in dry ether (100 mL) was cooled to 0 °C, and a solution of $AlCl_3$ (20 g, 0.15 mol) in dry ether (80 mL) was added dropwise. Then, the solution was stirred at 0 °C for 1 h and methyl (*E*)-2-heptenoate **2** (14.2 g, 0.1 mol) was added slowly. The mixture was stirred at 0 °C for 5 h. It was quenched by dropwise addition of water followed by 10% sodium bicarbonate. After filtration, the phases were separated, and the aqueous phase was extracted with ether. The combined organic phases were washed with brine and then dried over anhydrous $MgSO_4$. After evaporation of the solvent by rotary evaporation, the residue was distilled under reduced pressure to give (*E*)-2-heptenol **3** (9.7 g, 85%) as a colourless oil, b.p. 52–54 °C (1.32 kPa); ^{1}H NMR: δ 0.88 (3 H, t, *J* = 7.2 Hz), 1.22–1.43 (4 H, m), 1.92 (1 H, br), 2.03 (2 H, q, *J* = 6.9 Hz), 4.07 (2 H, d, *J* = 4.8 Hz), 5.65 (2 H, m); ^{13}C NMR: δ 13.8, 22.1, 31.2, 31.8, 63.3, 128.8, 133.0; GC/MS (EI) *m/z* (%) 41 (41), 55 (32), 57 (100), 68 (17), 81 (28), 96 (16, [M-18]$^+$). The ^{1}H NMR data were consistent with those described in the literature.[24]

(±)-2,3-Epoxy-1-heptanol **(±)-4**: A solution of *m*-CPBA (29.6 g, 70%, 0.12 mol) in CH_2Cl_2 (120 mL) was added to a solution of (*E*)-2-heptenol **3** (11.4 g, 0.1 mol) in CH_2Cl_2 (60 mL). The solution was stirred for 10 h at –25 °C. The mixture was quenched with 10% NaOH solution and extracted by CH_2Cl_2. The combined extracts were washed with saturated Na_2SO_3 and brine, dried over anhydrous $MgSO_4$, and concentrated. The residue was distilled under reduced pressure to afford (±)-2,3-epoxy-1-heptanol **4** (11 g, 85%) as a colourless oil, b.p. 55–57 °C (1.32 kPa); ^{1}H NMR: δ 0.90 (3 H, t, *J* = 7.2 Hz), 1.20–1.49 (4 H, m), 1.56 (2 H, m), 1.92 (1 H, br), 2.95 (2 H, m), 3.63 (1 H, d, *J* = 12.3 Hz), 3.92 (1 H, d, *J* = 12.3 Hz); ^{13}C NMR: δ 13.9, 22.4, 28.0, 31.2, 56.0, 58.5, 61.7. The NMR data were consistent with those described in the literature.[25]

(2R,3R)-2,3-Epoxy-1-heptanol **(2*R*,3*R*)-4**: The procedure used was similar to that used in our previous work.[26] Crushed 4Å molecular sieves were heated in a vacuum oven at 200 °C and 1 mmHg for at least 3 h. Dichloromethane was distilled over CaH_2. An oven-dried 250 mL three-necked round-bottomed flask equipped with a magnetic stirbar, pressure equalising addition funnel, thermometer, nitrogen inlet, and bubbler was charged with 4Å powered activated molecular sieves (4.0 g) and dry CH_2Cl_2 (200 mL). The flask was cooled to –20 °C. D-(–)-Diethyl tartrate (2.48 g, 0.012 mol) and Ti $(OPr^i)_4$ (2.84 g, 0.01 mol) were added sequentially *via* syringe with stirring. The reaction mixture was stirred at –20 °C as *t*-BuOOH (36.4 mL, 5.5 mol L^{-1} in decane) was added through the addition funnel over ~10 min. The resulting mixture was stirred at –20 °C for 1 h. (*E*)-2-Heptenol (11.4 g, 0.1 mol) was added dropwise over a period of 20 min, taking care to maintain the reaction temperature between –20 and –15 °C. The mixture was stirred for an additional 8 h at –20 to –15 °C and then warmed to ~0 °C. The reaction mixture was slowly poured into a beaker containing a precooled (0 °C) solution 200 mL (200 mL) of $FeSO_4.7H_2O$ (33 g, 0.12 mol) and citric acid monohydrate (12.6 g, 0.06 mol). The two-phase mixture was stirred for 40 min at 0 °C and then transferred to a separatory funnel. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 80 mL). The combined organic layers were treated with a precooled (0 °C) solution of 30% NaOH (w/v) in saturated brine (180 mL). The two-phase mixture was stirred vigorously for 1 h at 0 °C. The phases were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 80 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was distilled under reduced pressure to afford (2*R,3R*)-2,3-epoxy-1-heptanol as a colourless oil (10.8 g, 83%, 93% ee, t_R 20.80 min for its trifluoroacetate), b.p. 55–57 °C (1.32 kPa); $[\alpha]_D^{20} = +31.7^o$ (c 2.52, MeOH) [lit.[27], $[\alpha]_D^{20} = +32^o$ (c 1, MeOH)]. The spectroscopic properties of the optically active product were the same as for (±)-**4**.

(±)-2,3-Epithio-1-heptanol **(±)-5**: The procedure used was that reported by Gao and Sharpless.[21] To a suspension of (±)-2,3-epoxy-1-heptanol **4** (6.5 g, 0.05 mol) and thiourea (4.6 g, 0.06 mol) in dry THF (100 mL) was added Ti$(OPr^i)_4$ (18.2 mL, 0.06 mol) at room temperature under nitrogen. After addition, thiourea gradually dissolved and a clear solution formed. The mixture was stirred for 2 h. The solution was then diluted with ether (80 mL) and quenched with saturated aqueous $NaHCO_3$ solution. The resulting mixture was stirred vigorously for ~1 h as a white precipitate separated from solution. The mixture was filtered through a pad of Celite, and the residue was washed thoroughly with ether and CH_2Cl_2. The combined organic phases were then washed with water and brine and then dried over anhydrous $MgSO_4$. After solvent removal, the residue was purified by flash chromatography on silica gel (petroleum/EtOAc, 15 : 1) to afford (±)-2,3-epithio-1-heptanol **5** (5.9 g, 81%) as a colourless oil, ^{1}H NMR: δ 0.91 (3 H, t, *J* = 7.2 Hz), 1.23–1.61 (5 H, m), 1.71 (1 H, br), 1.83 (1 H, m), 2.83 (1 H, m), 2.98 (1 H, q, *J* = 4.8 Hz), 3.67 (1 H, dd, *J* = 12.0, 4.8 Hz), 3.89 (1 H, dd, *J* = 12.0, 4.2 Hz); ^{13}C NMR: δ 13.9, 22.2, 31.2, 35.2, 40.8, 44.6, 63.7; GC/MS (EI): *m/z* (%) 41 (59), 45 (36), 55 (38), 57 (41), 69 (33), 73 (100), 81 (59), 85 (32), 95 (67), 112 (38), 115 (41), 146 (57, M$^+$); HRESIMS, *m/z* 169.06542 [M + Na$^+$] (Calcd. for $C_7H_{14}NaOS$, 169.06576).

(2S,3S)-2,3-Epithio-1-heptanol **(2*S*,3*S*)-5**: Obtained by following the same experimental procedure as described above for (±)-**5**. (2*S*,3*S*)-**5** was obtained with 92% ee from (2*R,3R*)-**4** (94% ee, t_R 45.66 min for its trifluoroacetate). $[\alpha]_D^{20} = -119.5^o$ (c 2.75, $CHCl_3$). The spectroscopic properties of the optically active product were the same as for (±)-**5**.

(±)-3-Mercapto-1-heptanol **(±)-6**: To a solution of (±)-2,3-epithio-1-heptanol **5** (3.7 g, 0.025 mol) in dry THF (30 mL) was added a 65 wt% solution of Red-Al in toluene (15.6 mL, 0.05 mmol) dropwise under nitrogen at 0 °C. After stirring at room temperature for 6 h, the solution was diluted with ether and quenched with 5% HCl solution. After further stirring at room temperature for 30 min, the white precipitate formed was removed by filtration. The filtrate was extracted with CH_2Cl_2 (3 × 40 mL), The combined organic extracts were dried over anhydrous Na_2SO_4, filtered and concentrated. Purification by column chromatography on silica gel (petroleum/EtOAc, 15: 1) gave (±)-3-mercapto-1-heptanol **6** (2.2 g, 60%); ^{1}H NMR: δ 0.91 (3 H, t, *J* = 7.2 Hz), 1.20–1.45 (4 H, m), 1.40 (1 H, d, *J* = 7.5 Hz), 1.51 (1 H, m), 1.59–1.74 (3 H, m), 1.97 (1 H, m), 2.94 (1 H, m), 3.83 (2 H, m); ^{13}C NMR: δ 14.0, 22.4, 29.2, 38.1, 39.3, 41.3, 60.8; GC/MS (EI): *m/z* (%) 41 (57), 55 (100), 57 (56), 61 (45), 69 (44), 81 (70), 96 (29), 114 (69), 148 (28, M$^+$). NMR data were consistent with those described in the literature.[16]

(3S)-3-Mercapto-1-heptanol **(3*S*)-6**: Obtained by following the same experimental procedure as described above for (±)-**6**. (3*S*)-**6** was obtained with 92% ee (t_R 63.31 min) from (2*S*,3*S*)-**5** (92% ee). $[\alpha]_D^{20} = -1.3^o$ (c 2.65, $CHCl_3$) [lit.[16], $[\alpha]_D^{20} = +4.4^o$ (c 5.0, $CHCl_3$)]. The NMR data of the optically active products were the same as for (±)-**6**.

(±)-3-Mercapto-1-heptyl acetate **(±)-7**: A mixture of (±)-3-mercapto-1-heptanol **6** (1.5 g, 10 mmol) and acetic anhydride (1.2 g, 11 mmol) in pyridine (25 mL) was stirred for 8 h at –20 °C. Then the solution was poured into diluted HCl and extracted with CH_2Cl_2 (3 × 30 mL), The combined organic extracts were dried with anhydrous $MgSO_4$, filtered and concentrated. Purification by column chromatography on silica gel (petroleum/EtOAc, 15: 1) gave (±)-3-mercapto-1-heptyl acetate **7** (1.0 g, 53%); ^{1}H NMR: δ 0.91 (3 H, t, J = 7.2 Hz), 1.20–1.40 (3 H, m), 1.39 (1 H, d, J = 7.2 Hz), 1.44–1.60 (2 H, m), 1.60–1.80 (2 H, m), 1.95–2.08 (1 H, m), 2.05 (3 H, s), 2.85 (1 H, m), 4.24 (2 H, m); ^{13}C NMR: δ 13.9, 20.9, 22.3, 29.0, 37.5, 37.6, 38.7, 62.2, 170.9; GC/MS (EI): *m/z* (%) 43 (71), 55 (49), 69 (15), 73 (23), 88 (100), 97 (20), 101 (26), 130 (25, $[M-60]^+$). The NMR data were consistent with those described in the literature.[16]

(3S)-3-Mercapto-1-heptyl acetate **(3*S*)-7**: Obtained by following the same experimental procedure as described above for (±)-**7**. (3*S*)-**7** was obtained with 91% ee (t_R 65.61 min) from (3*S*)-**6** (92% ee). $[\alpha]_D^{20} = +7.0^o$ (c 2.10, $CHCl_3$) [lit.[16], $[\alpha]_D^{20} = +7.3^o$ (c 5.0, $CHCl_3$)]. The NMR data of the optically active products were the same as for (±)-**7**.

(3R)-3-Mercapto-1-heptanol **(3*R*)-6** *and its acetate* **(3*R*)-7**: Prepared by the similar approach as (3*S*)-**6** and (3*S*)-**7** except using L-(+)-diethyl tartrate as a chiral ligand in Sharpless AE. (3*R*)-**6**, 91% ee (t_R 63.97 min), $[\alpha]_D^{20} = +1.3^o$ (c 2.85, $CHCl_3$); (3*R*)-**7**, 90% ee (t_R 65.15 min), $[\alpha]_D^{20} = -7.0^o$ (c 2.05, $CHCl_3$) [lit.[16], $[\alpha]_D^{20} = -7.5^o$ (c 5.0, $CHCl_3$)].

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