Asymmetric Synthesis of Secondary Alcohols and 1,2-disubstituted Epoxide via Organocatalytic Sulfenylation.

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I. General experimental procedures

All glassware was thoroughly dried in an oven at 120°C prior to use. All reactions were carried out at atmospheric pressure, under argon, unless otherwise stated. Solvents and reagents were purchased from suppliers and used without any further purification. Normal phase silica gel (BDH) and sand (VWR) were used for flash chromatography (FC). All reactions monitored by TLC unless otherwise stated. TLC plates pre-coated with silica gel 60 F254 on aluminium (Merck KGaA) were used, detection was by UV (254 nm) or chemical stain (KMnO4 or PMA). High resolution mass spectrometry was performed using a VG70 SE instrument operating in modes CI (chemical ionisation), EI (electron ionisation), ESI (electrospray ionisation). NMR spectra were recorded at 300, 400, 500 and 600 MHz for 1H and at 75, 100, 125 and 150 MHz for 13C on Bruker instruments (AMX-300, AMX-400, AMX-500, AMX-600 respectively) at ambient temperature, unless otherwise stated; 19F and 31P NMR spectra were recorded on Bruker AMX-300 at 282 MHz and 121 MHz respectively; all chemical shifts were referenced to the residual proton impurity of the deuterated solvent. The multiplicity of the signal is indicated as s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), dd (double of doublets), dt (double of triplets), m (multiplet), defined as all multiplet signals where overlap or complex coupling of signals makes definitive descriptions of peaks difficult. All peaks should be taken as sharp unless otherwise described. Coupling constants are defined as $J$ and quoted in Hz to one decimal place. Infrared spectra were obtained on a Perkin Elmer Spectrum 100 FTIR Spectrometer operating in ATR mode. Room temperature is defined as between 19-22 ºC. Pet denotes for Petroleum Ether (40-60 ºC).

II. Synthesis of Aldehydes (1)

6,6-Dimethoxyhexanal^1

Ozone was bubbled through a solution of Cyclohexene (10.1 ml, 100 mmol) in CH$_2$Cl$_2$ (250 ml) and MeOH (50 ml) cooled to −78 ºC until a blue colour was noticed. Excess ozone was removed by bubbling oxygen through the reaction mixture then $p$-toluenesulfonic acid monohydrate (1.47 g, 7.70 mmol) was added and the reaction was allowed to warm to RT over 1.5 hr. Sodium bicarbonate (2.59 g, 30.8 mmol) was added and the resulting suspension was stirred for 15 minutes before adding dimethyl sulfide (16.0 ml, 200 mmol) and stirring the reaction mixture overnight at RT. The solvents were removed under reduced pressure and the crude residue was partitioned between CH$_2$Cl$_2$ and water. The organic layer was washed with brine, then dried over MgSO$_4$, filtered and evaporated to dryness. The crude oil was purified by column chromatography (Pet/EtOAc = 80/20) to afford the aldehyde (11.2 g, 69.9
mmol, 70%) as a colourless oil. $\nu_{\text{max}}$ (film/cm$^{-1}$) 2947, 1708, 1459, 1389, 1127; $\delta_{\text{H}}$ (400 MHz, CDCl$_3$) 1.37-1.45 (2H, m, CH$_2$), 1.60-1.72 (4H, m, 2 × CH$_2$), 2.46 (2H, td, $J = 7.4$, 1.6, CH$_2$CHO), 3.34 (6H, s, 2 × OCH$_3$), 4.38 (1H, t, $J = 5.7$, CH(OMe)$_2$), 9.79 (1H, t, $J = 1.6$, CHO); $\delta_{\text{C}}$ (100 MHz, CDCl$_3$) 21.9, 24.2, 32.3, 43.8, 52.8, 104.3, 202.4; Found (EI): [M-H]$^+$ 159.10249, C$_8$H$_{15}$O$_3$ requires 159.10212. These spectroscopic data are in agreement with those reported in literature.

5,5-Dimethoxypentanal$^2$

A solution of cyclopentene (8.8 ml, 100 mmol) in CH$_2$Cl$_2$ (250 ml) and MeOH (50 ml) was cooled to −78 °C and ozone was bubbled through it until a blue colour was observed. Excess ozone was removed by bubbling oxygen through the reaction mixture until a clear solution was obtained. $p$-Toluenesulfonic acid monohydrate (1.47 g, 7.7 mmol) was added and the solution was allowed to warm to RT over 1.5 hrs. Sodium bicarbonate (2.59 g, 30.8 mmol) was added and the mixture stirred for 15 minutes. The reaction was quenched with dimethylsulfide (16 ml, 200 mmol) and allowed to stir at RT for 16 hrs. The solvents were removed in vacuo and the residue was partitioned between CH$_2$Cl$_2$ (100 ml) and water (75 ml). The aqueous layer was extracted with CH$_2$Cl$_2$ (2 × 50 ml). The combined organic layers were washed with brine (100 ml), dried over MgSO$_4$, filtered and evaporated to dryness. The crude material was purified by column chromatography (Pet/EtOAc = 80/20) to afford the aldehyde as colourless oil (2.89 g, 19.8 mmol, 20%); $\delta_{\text{H}}$ (600 MHz, CDCl$_3$) 1.65 (2H, m, CH$_2$CH$_2$CH(OR)$_2$), 1.71 (2H, m, CH$_2$CH(OR)$_2$), 2.49 (2H, td, $J = 7.0$, 1.6, CH$_2$CHO), 3.33 (6H, s, 2 × OCH$_3$), 4.38 (1H, t, $J = 5.8$, CH(OMe)$_2$), 9.78 (1H, t, $J = 1.6$, CHO); $\delta_{\text{C}}$ (150 MHz, CDCl$_3$) 17.2, 31.8, 43.5, 52.7, 104.1, 202.3; Found (EI): [M+H]$^+$, 145.08521, C$_7$H$_{15}$O$_3$ requires 145.08592. These spectroscopic data are in agreement with those reported in literature.
III. Synthesis of Sulfenyl-triazoles (3)

1-(Phenylthio)-1H-1,2,4-triazole (3a)

Sulfuryl chloride (1 eq.) was added dropwise to a solution of diphenyl disulfide (1 eq.) in CH$_2$Cl$_2$ (1 M) stirred at RT. After stirring for 20 min, this solution was added to a second solution of 1,2,4-triazole (2.5 eq.) and NEt$_3$ (2.2 eq.) in CH$_2$Cl$_2$ (2.5 M). After 15 min the reaction mixture was concentrated *in vacuo*. The white solid residue was extracted with Pet and Pet:CH$_2$Cl$_2$ (7:3). The combined extracts were evaporated to dryness and purified by column chromatography (Pet:Et$_2$O 7:3 to 5:5) to afford the sulfenyl-triazole as a colourless oil (7.75 g, 4.37 mmol, 55%); $\delta$$_H$ (400 MHz, CDCl$_3$) 7.38-7.45 (5H, m, 5 × ArH), 8.09 (1H, s, 1 × HetH), 8.37 (1H, s, 1 × HetH), $\delta$$_C$ (125 MHz, CDCl$_3$) 129.4, 129.6, 129.8, 134.8, 151.0, 154.2, Found (CI): [M+H]$^+$ 178.04439, C$_8$H$_8$N$_3$S requires 178.04388. These spectroscopic data are in agreement with those reported in literature.

1-Hexylsulfanyl-1,2,4-triazole (3b)

Prepared according to the literature procedure; Colourless oil (4.49 g, 24.2 mmol, 61%); $\delta$$_H$ (400 MHz, CDCl$_3$) 0.89 (3H, t, J = 7.0, CH$_3$), 1.23-1.34 (4H, m, (CH$_2$)$_2$CH$_3$), 1.41 (2H, quint, J = 7.3, CH$_2$(CH$_2$)$_2$CH$_3$), 1.57 (2H, quint, J = 7.3, SCH$_2$CH$_2$), 3.05 (2H, t, J = 7.3, SCH$_2$), 8.06 (1H, s, HetH), 8.22 (1H, s, HetH); $\delta$$_C$ (125 MHz, CDCl$_3$) 14.0, 22.5, 27.9, 28.0, 31.3, 41.0, 151.5, 154.2; Found (EI): [M] 185.09867, C$_8$H$_{16}$N$_3$S requires 185.09812. These spectroscopic data are in agreement with those reported in literature.
IV. Synthesis of β-Hydroxysulfides (4-5)

A solution of aldehyde (1 eq.) and catalyst (S)-2 (0.1 eq.) was stirred in toluene (1.3 M) for 15 min. A solution of sulfonyl-triazole 3 (1.3 eq.) in toluene (1.6 M) was added dropwise and the resulting mixture was stirred under Argon at RT for 24 hrs. The reaction mixture was subsequently treated according to one of the following 3 different procedures

**Procedure A**

The reaction mixture was quickly filtered through a short pad of silica gel eluting with toluene. The fractions containing the product were combined and used in the following step. The concentration of α-sulfonylaldehyde in the toluene solution was determined each time by $^1$H-NMR.

**Procedure B**

The reaction mixture was quickly sucked under vacuum through a pre-wet (toluene) pad of silica (≈1.5 g per 100 mg of starting material) and washed with toluene (10 ml per 100 mg of starting material). The toluene solution of α-sulfonylaldehyde was used in directly in a reaction with NaBH$_4$ or an organometallic nucleophile.

**Procedure C**

The crude reaction mixture was taken onto the following step without further purification.

The toluene solution of the intermediate α-sulfonylaldehyde obtained via one of the 3 procedures described above was added dropwise to a (commercially available) solution of the organometallic reagent (3-4 eq.) cooled to −78 °C (for Li reagents) or −10 °C (for Grignard reagents). The reaction was monitored by TLC and stirred until all the intermediate α-sulfonylaldehyde was consumed. The reaction was quenched with sat NH$_4$Cl and partitioned between water and Et$_2$O. The aqueous layer was extracted with Et$_2$O and the combined organic layers were washed with brine, dried over MgSO$_4$, filtered and evaporated to dryness. The crude β-hydroxysulfide was purified by column chromatography (Pet/Et$_2$O).
(S)-6,6-Dimethoxy-2-(phenylthio)hexan-1-ol (4a)

A solution of sulfenyl triazole 3a (1.32 g, 7.49 mmol) in toluene (5 ml) was added to a solution of aldehyde 6,6-dimethoxyhexanal (1.00 g, 6.24 mmol) and catalyst (S)-2 (370 mg, 0.62 mmol) in toluene (5 ml) stirred at RT. The reaction mixture was stirred at RT for 16 hrs then diluted with MeOH (40 ml). Sodium borohydride (284 mg, 7.49 mmol) was added in portions and the mixture was stirred at RT for 20 min. The solvents were removed under reduced pressure and the crude material was purified by column chromatography (Pet/EtOAc = 70/30) to afford the alcohol (954 mg, 3.53 mmol, 57%) as a colourless oil; [α]D25 −6.0 (c. 1.0, CHCl3); νmax (film/cm−1) 3425, 3058, 2943, 2830, 1584, 1474, 1438, 1386, 1125, 1047; δH (400 MHz, CDCl3, 60 °C) 1.59–1.73 (6H, m, 3 × CH2), 2.07 (1H, br s, OH), 3.17 (1H, dtd, J = 12.5, 6.1, 4.6, SCH), 3.33 (3H, s, 1 × CH(OCH3)2), 3.34 (3H, s, 1 × CH(OCH3)2), 3.58 (1H, dd, J = 11.1, 6.1, CHHOH), 3.67 (1H, dd, J = 11.1, 4.6, CHHOH), 4.36 (1H, t, J = 5.2, CH(OCH3)2), 7.27–7.33 (3H, m, 3 × ArH), 7.46 (2H, m, 2 × ArH); δC (100 MHz, CDCl3, 60 °C) 22.1, 31.3, 32.4, 52.6, 52.7, 52.8, 64.1, 104.6, 127.3, 128.9, 132.7, 133.9; Found (EI): [M]+ 270.12867, C14H22O3S requires 270.12841.

(R)-3-Methyl-2-(phenylthio)butan-1-ol (4c)

Obtained via purification procedure A; 98:2 er; colourless oil (91 mg, 0.41 mmol, 62%). [α]D25 −8.3 (c. 1.0, CHCl3); νmax (film/cm−1) 3368, 3059, 2954, 2928, 2857, 1584, 1466, 1438, 1279, 1024; δH (600 MHz, CDCl3) 0.89 (3H, t, J = 7.0, CH3), 1.26-1.33 (4H, m, (CH2)2CH3), 1.42-1.65 (4H, m, CH(CH2)3), 1.99 (1H, br s, OH), 3.13-3.17 (1H, m, SCH), 3.50 (1H, dd, J = 11.4, 6.4, 1 × CHHOH), 3.62 (1H, dd, J = 11.4, 4.6, 1 × CHHOH), 7.26-7.31 (3H, m, 3 × ArH), 7.43-7.45 (2H, m, 2 × ArH); δC (150 MHz, CDCl3) 14.2, 22.6, 26.9, 31.3, 31.7, 52.9, 63.7, 127.6, 129.1, 133.0, 133.5; Found (EI): [M]+ 224.12321, C13H20OS requires 224.12294.
Obtained via purification procedure A (96:4 er) or C (>99:1 er); colourless oil (141 mg, 0.72 mmol, 62%); \([\alpha]^{20}_D +14.5\) (c. 0.05, CHCl\(_3\)); \(v_{\text{max}}\) (film/cm\(^{-1}\)) 3378, 3059, 2960, 2930, 2873, 1584, 1478, 1438, 1386, 1367, 1385, 1063, 1025; \(\delta_H\) (600 MHz, CDCl\(_3\)) 1.06 (3H, d, \(J = 6.8\), 1 \(\times\) CH\(_3\)), 1.08 (3H, d, \(J = 6.8\), 1 \(\times\) CH\(_3\)), 1.90 (1H, br s, OH), 2.01 (1H, septt, \(J = 6.8\), 6.3, CH(CH\(_3\))\(_2\)), 3.06 (1H, dd, \(J = 11.6\), 7.2, CHOH), 3.74 (1H, dd, \(J = 11.6\), 5.1, CHOH); \(\delta_C\) (150 MHz, CDCl\(_3\)) 20.0, 20.5, 29.9, 60.9, 62.6, 127.2, 129.1, 132.2, 135.2; Found (EI): [M]+ 196.09200, C\(_{11}\)H\(_{16}\)OS requires 196.09164.

\((2R,3S)-3-(\text{Phenylthio})\text{octan-2-ol (5a)}\)

Obtained via purification procedure A; colourless oil (180 mg, 0.75 mmol, 94%). \([\alpha]^{20}_D -4.2\) (c. 1.0, CHCl\(_3\)); \(v_{\text{max}}\) (film/cm\(^{-1}\)) 3414, 3060, 2959, 2929, 2858, 1584, 1466, 1439, 1279, 1139. Isolated as a 91:9 mixture of diastereoisomers; major isomer \(\delta_H\) (600 MHz, CDCl\(_3\)) 0.88 (3H, t, \(J = 6.8\), CH\(_3\)CH\(_3\)), 1.19 (3H, d, \(J = 6.4\), CHCH\(_3\)), 1.27-1.71 (8H, m, 4 \(\times\) CH\(_2\)), 2.33 (1H, br s, OH), 3.16 (1H, ddd, \(J = 9.4\), 5.8, 3.2, SCH), 3.89 (1H, dd, \(J = 6.4\), 3.2, CHOH), 7.22-7.30 (3H, m, 3 \(\times\) ArH), 7.44 (2H, d, \(J = 7.7\), 2 \(\times\) ArH); \(\delta_C\) (150 MHz, CDCl\(_3\)) 14.2, 19.1, 22.6, 27.5, 30.1, 31.8, 58.7, 68.3, 127.1, 129.2, 132.0, 135.5; minor isomer \(\delta_H\) (600 MHz, CDCl\(_3\)) 0.88 (3H, t, \(J = 6.8\), CH\(_3\)CH\(_3\)), 1.25 (3H, d, \(J = 6.1\), CHCH\(_3\)), 1.27-1.71 (8H, m, 4 \(\times\) CH\(_2\)), 2.91 (1H, ddd, \(J = 9.6\), 6.5, 3.2, SCH), 3.72 (1H, dq, \(J = 6.5\), 6.1, CHOH), 7.22-7.30 (3H, m, 3 \(\times\) ArH), 7.44 (2H, d, \(J = 7.7\), 2 \(\times\) ArH); \(\delta_C\) (150 MHz, CDCl\(_3\)) 14.2, 20.2, 22.7, 27.0, 30.1, 31.1, 59.3, 68.3, 127.3, 129.1, 132.5, 135.5, Found (EI): [M]+ 238.13884, C\(_{14}\)H\(_{22}\)OS requires 238.13859.

\((1R,2S)-1\text{-cyclohexyl-2-(phenylthio)heptan-1-ol (5b)}\)

Obtained via purification procedure A; colourless oil (64 mg, 0.21 mmol, 48%); \([\alpha]^{25}_D -13.2\) (c. 0.33, CHCl\(_3\)); \(v_{\text{max}}\) (film/cm\(^{-1}\)) 3471, 3060, 2959, 2853, 1584, 1449, 1439, 1279, 1139. Isolated as a 98:2 mixture of diastereoisomers, major isomer \(\delta_H\) (600 MHz, CDCl\(_3\)) 0.78-0.90 (2H, m, 2 \(\times\) cHex), 0.90 (3H, t, \(J = 7.1\), CH\(_3\)), 1.04-1.73 (17H, m, 9 \(\times\) cHex, 4 \(\times\) CH\(_2\)), 2.01 (1H, br d, \(J = 12.9\), 1 \(\times\) cHex), 2.45 (1H, d, \(J = 2.6\), OH), 3.23 (1H, dt, \(J = 8.4\), 2.4, SCH), 3.30-3.33 (1H, m, OCH), 7.21-7.40 (5H, m, 5 \(\times\) cHex).
ArH); \( \delta_C \) (150 MHz, CDCl\textsubscript{3}) 14.2, 22.7, 25.9, 26.0, 26.4, 27.1, 27.6, 28.8, 30.1, 31.8, 39.6, 54.0, 76.0, 127.1, 129.2, 131.9, 134.8; minor isomer \( \delta_H \) (600 MHz, CDCl\textsubscript{3}) 0.78-0.90 (2H, m, 2 × cHex), 0.90 (3H, t, \( J = 7.1 \), CH\textsubscript{3}), 1.04-1.73 (17H, m, 9 × cHex, 4 × CH\textsubscript{2}), 1.83 (1H, br d, \( J = 13.2 \), 1 × cHex), 2.45 (1H, d, \( J = 2.6 \), OH), 3.17-3.20 (1H, m, Sch), 3.27-3.29 (1H, m, OCH), 7.21-7.40 (5H, m, 5 × ArH); \( \delta_C \) (150 MHz, CDCl\textsubscript{3}) 14.2, 22.8, 26.2, 26.3, 26.5, 27.1, 27.3, 30.4, 31.7, 32.4, 40.7, 55.3, 75.9, 127.3, 129.0, 132.8, 137.1; Found (EI): [M]+ 306.20106, C\textsubscript{19}H\textsubscript{30}OS requires 306.20119.

(1R,2S)-1-Cyclopropyl-2-(phenylthio)heptan-1-ol (5c)

![Structure of 1R,2S-1-Cyclopropyl-2-(phenylthio)heptan-1-ol (5c)](image)

Obtained via purification procedure A; colourless oil (161 mg, 0.61 mmol, 76%). \([\alpha]_D^{25} -1.5 \) (c. 1.0, CHCl\textsubscript{3}); \( \nu_{max} \) (film/cm\textsuperscript{-1}) 3437, 3004, 2955, 2928, 2858, 1584, 1479, 1466, 1438, 1279, 1025; Isolated as a 93:7 mixture of diastereoisomers, major isomer \( \delta_H \) (600 MHz, CDCl\textsubscript{3}) 0.09-0.14 (1H, m, 1 × cPr), 0.32 (1H, app sext, \( J = 4.9 \), 1 × cPr), 0.47-0.57 (2H, m, 2 × cPr), 0.88 (3H, t, \( J = 6.8 \), CH\textsubscript{3}), 0.99 (1H, qt, \( J = 8.2, 4.9, cp\text{PrH-CHOH} \)), 1.26-1.90 (8H, m, 4 × CH\textsubscript{2}), 2.37 (1H, br s, OH), 2.93-2.95 (1H, m, Sch), 3.31 (1H, m, OCH), 7.19-7.43 (5H, m, 5 × ArH); \( \delta_C \) (150 MHz, CDCl\textsubscript{3}) 2.8, 3.2, 13.9, 14.2, 22.6, 27.6, 29.8, 31.8, 57.3, 76.9, 127.0, 129.1, 131.7, 135.6; minor isomer \( \delta_H \) (600 MHz, CDCl\textsubscript{3}) 0.23-0.27 (1H, m, 1 × cPr), 0.35-0.38 (1H, m, 1 × cPr), 0.45-0.55 (2H, m, 2 × cPr), 0.85-2.87 (1H, m, Sch), 3.16 (1H, m, OCH), 7.19-7.45 (5H, m, 5 × ArH); \( \delta_C \) (600 MHz, CDCl\textsubscript{3}) 2.9, 3.7, 14.2, 15.8, 22.7, 27.2, 31.7, 31.9, 57.9, 77.8, 127.1, 129.0, 132.1, 135.0; Found (EI): [M]+ 264.15388, C\textsubscript{16}H\textsubscript{24}OS requires 264.15424.

(6R,7S)-7-(Phenylthio)dodecan-6-ol (5d)

![Structure of 6R,7S-7-(Phenylthio)dodecan-6-ol (5d)](image)

Obtained via purification procedure A; colourless oil (155 mg, 0.53 mmol, 66%). \([\alpha]_D^{25} -1.2 \) (c. 1.0, CHCl\textsubscript{3}); \( \nu_{max} \) (film/cm\textsuperscript{-1}) 3446, 3060, 2955, 2929, 2858, 1468, 1439, 1374, 1277, 1175, 1137. Isolated as a 97:3 mixture of diastereoisomers; major isomer \( \delta_H \) (600 MHz, CDCl\textsubscript{3}) 0.86 (3H, m, 1 × C\textsubscript{H3}), 1.21-1.73 (16H, m, 8 × CH\textsubscript{2}), 3.18 (1H, dt, \( J = 9.8, 3.3 \), Sch), 3.62-3.65 (1H, m, OCH), 7.22-7.45 (5H, m, 5 × ArH); \( \delta_C \) (150 MHz, CDCl\textsubscript{3}) 14.2, 22.6, 22.7, 26.0, 27.5, 29.2, 31.8, 31.9, 33.1, 57.4, 72.2, 127.1, 129.1, 132.0, 135.3; minor isomer \( \delta_H \) (600 MHz, CDCl\textsubscript{3}) 0.86-0.92 (6H, m, 2 × CH\textsubscript{3}), 1.21-1.73 (16H, m, 8 × CH\textsubscript{2}), 2.98-3.02 (1H, m, Sch), 3.53-3.56
(1H, m, OCH), 7.22-7.45 (5H, m, 5 × ArH); δC (150 MHz, CDCl₃) 14.2, 22.6, 22.7, 25.7, 27.1, 29.3, 31.6, 31.9, 34.3, 57.9, 73.2, 127.2, 129.0, 132.4, 135.0; Found (EI): [M]+ 294.20131, C₁₈H₃₀OS requires 294.20119.

(5R,6S)-6-(Phenylthio)octan-5-ol (5e)

Obtained via purification procedure B; colourless oil (89 mg, 0.32 mmol, 56%); [α]²⁵D −2.7 (c. 0.30, CHCl₃); ν max (film/cm⁻¹) 3443, 3061, 2958, 1584, 1466, 1439, 1279, 1025. Isolated as a 98:2 mixture of diastereoisomers; major isomer δH (600 MHz, CDCl₃) 0.87-0.90 (6H, m, 2 × C₇H₃), 1.22-1.73 (14H, m, 7 × C₇H₂), 2.08 (1H, br s, OH), 3.18 (1H, ddd, J = 9.7, 3.7, 3.2, SCHR), 3.62-3.65 (1H, m, OCH), 7.22-7.30 (3H, m, 3 × ArH); δC (150 MHz, CDCl₃) 14.2, 22.6, 22.7, 25.7, 27.1, 29.3, 31.6, 34.3, 57.9, 73.2, 127.2, 129.0, 132.4, 135.0; minor isomer δH (600 MHz, CDCl₃) 0.85-0.90 (6H, m, 2 × C₇H₃), 1.22-1.73 (14H, m, 7 × C₇H₂), 2.99-3.03 (1H, m, SCHR), 3.55 (1H, ddd, J = 9.1, 5.8, 3.7, OCH), 7.22-7.43 (5H, m, 5 × ArH); δC (150 MHz, CDCl₃) 14.2, 14.3, 22.7, 22.8, 27.1, 28.2, 29.2, 31.6, 34.1, 57.9, 73.2, 127.2, 129.0, 132.4, 135.0; Found (CI): [M+H]+ 280.18589, C₁₇H₂₈OS requires 280.18554.

(1R,2S)-1-phenyl-2-(phenylthio)heptan-1-ol (5f)

Obtained via purification procedure A; colourless oil (168 mg, 0.56 mmol, 70%); 5f [α]²⁵D +39.3 (c. 1.0, CHCl₃); ent-5f [α]²⁵D −43.7 (c.1.0, CHCl₃); ν max (film/cm⁻¹) 3450, 3061, 3029, 2955, 2928, 2858, 1584, 1452, 1439, 1279, 1179, 1139. Isolated as a 99:1 mixture of diastereoisomers; major isomer δH (600 MHz, CDCl₃) 0.83 (3H, t, J = 7.1, C₇H₃), 1.10-1.63 (8H, 4 × C₇H₂), 2.81 (1H, br s, OH), 3.38 (1H, dt, J = 10.1, 3.2, SCHR), 4.78 (1H, d, J = 3.2, OCHR), 7.23-7.49 (5H, m, 5 × ArH); δC (150 MHz, CDCl₃) 14.1, 22.5, 27.4, 27.5, 31.6, 58.2, 73.5, 126.1, 127.4, 127.5, 128.3, 129.3, 132.4, 134.8, 140.9; minor isomer δH (600 MHz, CDCl₃) 0.81 (3H, t, J = 7.1, C₇H₃), 1.10-1.63 (8H, 4 × C₇H₂), 2.74 (1H, br s, OH), 3.14 (1H, ddd, J = 9.8, 8.5, 3.4, SCHR), 4.42 (1H, d, J = 8.5, OCHR), 7.20-7.47 (5H, m, 5 × ArH); δC (150 MHz, CDCl₃) 14.1, 22.5, 26.8, 30.9, 31.5, 59.9, 75.8, 127.2, 127.8, 128.1, 128.5, 129.1, 133.1, 133.5, 141.3; Found (EI): [M]+ 300.15449, C₁₉H₂₉OS requires 300.15424.
(1S,2R)-1-cyclohexyl-3-phenyl-2-(phenylthio)propan-1-ol (5g)

Obtained via purification procedure B; colourless oil (124 mg, 0.38 mmol, 38%); [\(\alpha\)]\(_D^{25}\) = -65.7 (c. 1.0, CHCl\(_3\)); \(v\)\(_{\text{max}}\) (film/cm\(^{-1}\)) 3467, 3062, 3027, 2924, 2852, 1583, 1496, 1479, 1451, 1439, 1026. Isolated as a 98:2 mixture of diastereoisomers; major isomer \(\delta\)\(_H\) (600 MHz, CDCl\(_3\)) 0.85-1.27 (5H, m, 5 \times cHex), 1.62-1.72 (5H, m, 5 \times cHex), 2.05 (1H, br d, \(J = 12.8\), 1 \times cHex), 2.70 (1H, dd, \(J = 14.8\), 10.8, PhCHH), 3.14 (1H, dd, \(J = 14.8\), 3.5, PhCHH), 3.43 (1H, dd, \(J = 8.5\), 2.7, OCH), 3.59 (1H, ddd, \(J = 10.8\), 3.5, 2.7, SCH), 7.20-7.33 (10H, m, 10 \times ArH); \(\delta\)\(_C\) (150 MHz, CDCl\(_3\)) 25.9, 26.0, 26.4, 28.9, 30.1, 33.8, 39.7, 55.7, 76.1, 126.5, 127.2, 128.5, 129.1, 129.3, 132.0, 134.5, 139.7; minor isomer \(\delta\)\(_H\) (600 MHz, CDCl\(_3\)) 0.85-1.27 (5H, m, 5 \times cHex), 1.62-1.72 (5H, m, 5 \times cHex), 1.96 (1H, br d, \(J = 12.7\), 1 \times cHex), 2.96 (1H, dd, \(J = 14.0\), 10.8, PhCHH), 3.07 (1H, dd, \(J = 14.0\), 8.1, PhCHH), 3.27 (1H, dd, \(J = 8.0\), 3.3, OCH), 3.49 (1H, ddd, \(J = 8.1\), 7.2, 3.3, SCH), 7.20-7.33 (10H, m, 10 \times ArH); \(\delta\)\(_C\) (150 MHz, CDCl\(_3\)) 25.9, 26.0, 26.2, 28.7, 29.8, 34.3, 41.2, 55.9, 76.6, 126.5, 127.3, 128.4, 129.1, 129.4, 132.7, 135.0, 139.4. Found (EI): [M]\(^+\) 326.16966, C\(_{21}\)H\(_{26}\)OS requires 326.16989.

(1S,2R)-1-phenyl-2-(phenylthio)pent-4-en-1-ol (5h)

Obtained via purification procedure B; pale yellow oil (109 mg, 0.40 mmol, 34%); [\(\alpha\)]\(_D^{25}\) = -5.3 (c. 1.0, CHCl\(_3\)); \(v\)\(_{\text{max}}\) (film/cm\(^{-1}\)) 3448, 3062, 3029, 2978, 2921, 1640, 1583, 1494, 1478, 1452, 1438, 1025. Isolated as a single diastereoisomer: \(\delta\)\(_H\) (600 MHz, CDCl\(_3\)) 2.22-2.36 (2H, m, CH\(_2\)), 3.46 (1H, dt, \(J = 9.5\), 3.8, SCH), 4.80 (1H, d, \(J = 3.8\), OCH), 5.00-5.06 (2H, m, CH=CH\(_2\)), 5.84 (1H, dddd, \(J = 17.1\), 9.8, 7.3, 6.5, CH=CH\(_2\)), 7.24-7.48 (10H, m, 10 \times ArH); \(\delta\)\(_C\) (150 MHz, CDCl\(_3\)) 32.3, 57.5, 73.3, 117.3, 126.2, 127.6, 128.4, 128.9, 129.3, 132.5, 134.3, 135.8, 140.7. Found (EI): [M]\(^+\) 270.10694, C\(_{17}\)H\(_{18}\)OS requires 270.10729.
(1S,2R)-1-cyclohexyl-2-(phenylthio)pent-4-en-1-ol (5i)

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\text{\large \includegraphics[width=0.2\textwidth]{image}}
\]

Obtained via purification procedure B; pale yellow oil (120 mg, 0.44 mmol, 36%); \([\alpha]_D^{25} -8.9\) (c. 1.0, CHCl\(_3\)); \(\nu_{\text{max}}\) (film/cm\(^{-1}\)) 3466, 3074, 2924, 2851, 1640, 1583, 1449, 1439, 1025. Isolated as a 96:4 mixture of diastereoisomers: major isomer \(\delta_1\) (600 MHz, CDCl\(_3\)) 0.84-1.27 (5H, m, 5 × cHex), 1.54-1.70 (5H, m, 5 × cHex), 1.98-2.01 (1H, m, 1 × cHex), 2.26-2.32 (1H, m, 1 × CHHCH=CH\(_2\)), 2.49-2.54 (1H, m, 1 × CHHCH=CH\(_2\)), 3.28 (1H, dd, \(J = 8.0, 3.2, \text{OCH}\)), 3.39 (1H, dt, \(J = 9.8, 3.2, \text{SCH}\)), 5.11 (1H, d, \(J = 10.1, \text{CH}=\text{CHCH}=\text{CH}\(_2\)), 5.16 (1H, dq, \(J = 17.0, 1.6, \text{CH}=\text{CHCH}=\text{CH}\(_2\)), 6.00 (1H, ddt, \(J = 17.0, 10.1, 7.0, \text{CH}=\text{CH}\(_2\)), 7.23-7.40 (5H, m, 5 × ArH); \(\delta\)\(_C\) (150 MHz, CDCl\(_3\)) 25.9, 26.1, 26.4, 28.9, 32.1, 39.8, 53.1, 75.9, 117.1, 127.3, 129.2, 132.0, 134.5, 136.3; minor isomer \(\delta_1\) (600 MHz, CDCl\(_3\)) 0.84-1.27 (5H, m, 5 × cHex), 1.54-1.70 (5H, m, 5 × cHex), 1.89-1.91 (1H, m, 1 × cHex), 2.36-2.41 (1H, m, 1 × CHHCH=CH\(_2\)), 2.49-2.54 (1H, m, 1 × CHHCH=CH\(_2\)), 3.35 (1H, pd, \(J = 7.0, 4.7, \text{OCH}\)), 3.40-3.44 (1H, m, SCH), 5.10-5.34 (2H, m, CH=CH\(_2\)), 5.91 (1H, ddt, \(J = 17.1, 10.1, 7.0, \text{CH}=\text{CH}\(_2\)), 7.23-7.40 (5H, m, 5 × ArH); \(\delta\)\(_C\) (150 MHz, CDCl\(_3\)) 26.1, 26.2, 26.4, 27.9, 30.0, 37.2, 40.7, 54.0, 76.8, 117.5, 127.4, 129.1, 132.8, 135.8, 137.0; Found (EI): [M]\(^+\) 276.15465, C\(_{17}\)H\(_{24}\)OS requires 276.15424.

(3S,4R)-2-methyl-4-(phenylthio)hepta-1,6-dien-3-ol (5j)

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\text{\large \includegraphics[width=0.2\textwidth]{image}}
\]

Obtained via purification procedure B; colourless oil (91 mg, 0.39 mmol, 33%); \([\alpha]_D^{25} +3.5\) (c. 1.0, CHCl\(_3\)); \(\nu_{\text{max}}\) (film/cm\(^{-1}\)) 3447, 3074, 2924, 1639, 1583, 1478, 1439, 1279; isolated as a 90:10 mixture of diastereoisomers: major isomer \(\delta_1\) (400 MHz, CDCl\(_3\)) 1.68 (3H, s, CH\(_3\)), 2.24-2.31 (1H, m, SCHCH\(_2\)), 2.46-2.53 (1H, m, SCHCH\(_2\)), 3.37 (1H, dt, \(J = 9.4, 3.7, \text{SCH}\)), 4.11 (1H, d, \(J = 3.7, \text{OCH}\)), 5.00-5.17 (4H, m, 2 × CH=CH\(_2\)), 6.00 (1H, dddd, \(J = 17.0, 13.9, 10.2, 7.0, \text{CH}=\text{CH}\(_2\)), 7.26-7.52 (5H, m, 5 × ArH); \(\delta\)\(_C\) (150 MHz, CDCl\(_3\)) 19.4, 32.2, 53.4, 74.4, 112.7, 117.2, 127.6, 129.2, 132.5, 134.2, 136.1, 143.2; minor isomer \(\delta_1\) (400 MHz, CDCl\(_3\)) 1.74 (3H, s, CH\(_3\)), 2.14-2.21 (1H, m, SCHCH\(_2\)), 2.37-2.44 (1H, m, SCHCH\(_2\)), 3.14 (1H, dddd, \(J = 8.6, 8.0, 4.9, \text{SCH}\)), 3.95 (1H, d, \(J = 8.0, \text{OCH}\)), 5.00-5.17 (4H, m, 2 × CH=CH\(_2\)), 5.91-6.00 (1H, m, CH=CH\(_2\)), 7.26-7.52 (5H, m, 5 × ArH); \(\delta\)\(_C\) (150 MHz, CDCl\(_3\)) 17.3, 35.8, 55.0, 76.5, 115.1, 117.6, 128.0, 129.1, 133.9, 134.2, 135.4, 143.9; Found (EI): [M]\(^+\) 234.10761, C\(_{14}\)H\(_{16}\)OS requires 234.10729.
(1S,2R)-3-methyl-1-phenyl-2-(phenylthio)butan-1-ol (5k)

Obtained via purification procedure B; colourless oil (193 mg, 0.71 mmol, 61%); \([\alpha]_D^{25} -6.4\) (c 1.0, CHCl$_3$); \(\nu_{\text{max}}\) (film/cm$^{-1}$) 3431, 3061, 3031, 2960, 2927, 2871, 1583, 1478, 1454, 1439, 1383, 1026; isolated as a 87:13 mixture of diastereoisomers: major isomer \(\delta_\text{H}\) (400 MHz, CDCl$_3$) 1.08 (3H, d, \(J = 6.8\), 1 × C$_2$H$_3$), 1.14 (3H, d, \(J = 6.8\), 1 × C$_2$H$_3$), 2.23 (1H, septd, \(J = 6.8\), 3.2, C$_3$H$_7$(CH$_3$)$_2$), 2.64 (1H, br s, OH), 3.29 (1H, dd, \(J = 6.4\), 3.2, SCH), 4.84 (1H, d, \(J = 6.4\), OCH), 7.19-7.37 (10H, m, 10 × ArH); \(\delta_\text{C}\) (100 MHz, CDCl$_3$) 18.2, 22.5, 27.9, 65.7, 75.0, 126.7, 126.9, 127.5, 128.1, 128.8, 132.3, 135.7, 141.8; minor isomer \(\delta_\text{H}\) (400 MHz, CDCl$_3$) 1.02 (3H, d, \(J = 6.7\), 1 × C$_2$H$_3$), 1.03 (3H, d, \(J = 6.7\), 1 × C$_2$H$_3$), 1.80 (1H, septd, \(J = 6.7\), 3.2, CH(CH$_3$)$_2$), 3.28 (1H, dd, \(J = 8.6\), 3.2, SCH), 4.72 (1H, d, 8.6, OCH), 7.24-7.50 (10H, m, 10 × ArH); \(\delta_\text{C}\) (100 MHz, CDCl$_3$) 17.4, 21.4, 29.8, 69.1, 75.3, 126.7, 126.8, 128.0, 129.0, 131.3, 135.5, 143.1; Found (EI): [M]$^+$ 272.40544, C$_{17}$H$_{20}$OS requires 272.40510.

(2R,3S)-3-Hexylsulfanyl-6,6-dimethoxyhexan-2-ol (5l)

Catalyst (S)-2 (817 mg, 1.37 mmol) was added to a solution of 5,5-dimethoxypentanal (2.00 g, 13.7 mmol) in dry toluene (15 ml) and the solution was stirred at RT for 20 min. A solution of sulfenyl-triazole 3b (3.04 g, 16.4 mmol) in toluene (15 ml) was added dropwise and the reaction mixture was stirred at RT for 4 hrs under Argon.

The reaction mixture was partitioned between Et$_2$O (50 ml) and water (50 ml) and extracted with Et$_2$O (2 × 50 ml). Combined organic layers were washed with brine, dried over MgSO$_4$, filtered and evaporated to dryness. The residue was filtered through a silica plug (Pet/EtOAc = 85/15). The crude aldehyde was dissolved in anhydrous THF (60 ml) and added using a syringe pump to a solution of MeLi (1.6 M in THF, 21.4 ml, 34.3 mmol) cooled to −78 °C over 2 hrs. The reaction was stirred at −78 °C for 1 hr then quenched with sat. NH$_4$Cl (50 ml) and allowed to warm to RT. The mixture was then extracted with Et$_2$O (2 × 50 ml). The combined organic layers were washed with brine (50 ml), dried over MgSO$_4$, filtered and evaporated to dryness. The residue was purified by column chromatography (Pet/ Et$_2$O = 60/40) to afford the alcohol as a pale yellow oil (3.01 g, 10.8 mmol, 79%); \([\alpha]_D^{25} -5.4\) (c 1.0, CH$_2$Cl$_2$); \(\nu_{\text{max}}\) (film/cm$^{-1}$) 3454, 2927, 1454, 1379, 1280, 1171, 1053; the product was isolated as a 90:10 mixture of diastereoisomers: major isomer \(\delta_\text{H}\) (600 MHz, DMSO-d$_6$)
0.86 (3H, t, \(J = 6.8\), \(\text{CH}_2\text{CH}_3\)), 1.13 (3H, d, \(J = 6.1\), CHCH\(_3\)), 1.22-1.37 (7H, m, (CH\(_2\))\(_3\)CH\(_3\) and SCHCH\(_H\)), 1.45-1.52 (2H, m, SCH\(_2\text{CH}_3\)), 1.54-1.59 (1H, m, CHHCH(OR)\(_2\)), 1.63-1.68 (1H, m, SCHCH\(_H\)), 1.78-1.84 (1H, m, CHHCH(OR)\(_2\)), 2.42 (1H, ddd, \(J = 11.5, 5.9, 3.7\), SCH\(_H\)), 2.46-2.55 (2H, m, SCH\(_2\)), 3.20 (3H, s, 1 × OC\(_3\text{H}_3\)), 3.21 (3H, s, 1 × OC\(_3\text{H}_3\)), 3.63 (1H, dq, \(J = 11.5, 6.1\), C\(_\text{H}OH\)), 4.34 (1H, t, \(J = 5.6\), CH(OCH\(_3\))\(_2\)), 4.62 (1H, d, \(J = 5.3\), OH); \(\delta_c\) (150 MHz, DMSO-\(d_6\)) 14.4, 21.1, 22.5, 26.1, 28.4, 30.0, 30.3, 31.3, 31.5, 52.8, 69.6, 104.2; minor isomer \(\delta_H\) (600 MHz, DMSO-\(d_6\)) 0.86 (3H, t, \(J = 6.8\), CH\(_2\text{CH}_3\)), 1.07 (3H, d, \(J = 6.3\), CHCH\(_3\)), 1.22-1.37 (2H, m, (CH\(_2\))\(_3\)CH\(_3\) and SCHCH\(_H\)), 1.69-1.74 (1H, m, SCHCH\(_H\)), 2.46-2.55 (2H, m, SCH\(_2\)), 2.60-2.63 (1H, m, SCH\(_H\)), 3.20 (3H, s, 1 × OCH\(_3\)), 3.21 (3H, s, 1 × OCH\(_3\)), 3.76-3.81 (1H, m, OCH\(_3\)), 4.32 (1H, t, \(J = 5.7\), CH(OCH\(_3\))\(_2\)), 4.63 (1H, d, \(J = 5.0\), OH); \(\delta_c\) (150 MHz, DMSO-\(d_6\)) 13.9, 20.0, 22.6, 26.2, 28.6, 30.0, 30.4, 31.0, 32.2, 51.8, 55.2, 55.8, 69.1, 104.0; Found (FAB): [M-Na\(^+\)], 301.18156, C\(_{14}\)H\(_{30}\)O\(_3\)SNa requires 301.18133.

V. Synthesis of Enantoienriched alcohols

General procedure for the synthesis of secondary alcohols

A solution of \(\beta\)-hydroxysulfide (1 mmol) and Raney-Ni (2 g) in EtOH (0.05 M) was stirred at reflux for 2-4 hr. The mixture was cooled to RT and filtered through a pad of Celite®. The filtrate was evaporated to dryness to afford the crude alcohol.

\((R)\)-Octan-2-ol (6a)\(^6\)

\[
\begin{array}{c}
\text{OH} \\
\text{R}^1 \quad \text{R}^2
\end{array}
\]

\[
\begin{array}{c}
\text{R}^1 \quad \text{R}^2
\end{array}
\]

Obtained following the general procedure (51 mg, 0.40 mmol, 93%) (86:14 er); \([\alpha]_D^{25} = 5.4\) (c. 1.0, CHCl\(_3\)); \(\nu_{max}\) (film/cm\(^{-1}\)) 3339, 2960, 2927, 2857, 1462, 1373, 1279, 1177, 1141, 1115; \(\delta_H\) (400 MHz, CDCl\(_3\)) 0.91 (3H, t, \(J = 6.9\), CH\(_2\text{CH}_3\)), 1.21 (3H, d, \(J = 6.1\), CHCH\(_3\)), 1.27-1.51 (10 H, m, 5 × CH\(_2\)), 3.81 (1H, m, CHOH); \(\delta_c\) (100 MHz, CDCl\(_3\)) 14.1, 22.6, 23.5, 25.7, 29.3, 31.8, 39.4, 68.2. These spectroscopic data are in agreement with those reported in the literature.
(S)-1-cyclohexylheptan-1-ol (6b)$^7$

![Structure of (S)-1-cyclohexylheptan-1-ol](image)

Obtained following the general procedure (22 mg, 0.11 mmol, 90%) (92:8 er); $[\alpha]_{D}^{25} -10.5$ (c. 0.20, CHCl$_3$); $\nu_{\text{max}}$ (film/cm$^{-1}$) 3370, 2926, 2854, 1450, 1373, 1279, 1141; $\delta_{\text{H}}$ (600 MHz, CDCl$_3$) 0.88 (3H, t, J = 6.9, C$_3$H$_3$), 0.96-1.81 (21H, 11 × C$_6$H$_{15}$, 5 × CH$_2$), 3.33-3.35 (1H, m, OC$_3$H); $\delta_{\text{C}}$ (150 MHz, CDCl$_3$) 14.2, 22.8, 26.0, 26.3, 26.5, 26.7, 27.8, 29.4, 29.6, 32.0, 34.3, 43.7, 76.4. These spectroscopic data are in agreement with those reported in the literature.

(5)-1-cyclopropylheptan-1-ol (6c)$^8$

![Structure of (S)-1-cyclopropylheptan-1-ol](image)

Obtained following the general procedure (20 mg, 0.13 mmol, 56%) (88:12 er); $[\alpha]_{D}^{25} -5.5$ (c. 0.30, CHCl$_3$); $\nu_{\text{max}}$ (film/cm$^{-1}$) 3360, 2957, 2927, 2857, 1461, 1372, 1279, 1177, 1141; $\delta_{\text{H}}$ (600 MHz, CDCl$_3$) 0.18-0.27 (2H, m, 2 × cPr), 0.45-0.54 (2H, m, 2 × cPr), 0.88 (3H, t, J = 7.1, CH$_3$), 1.24-1.61 (11H, m, 5 × CH$_2$, 1 × cPr), 2.84 (1H, app q, J = 7.0, OCH); $\delta_{\text{C}}$ (150 MHz, CDCl$_3$) 2.5, 2.9, 14.2, 18.1, 22.8, 25.8, 29.5, 32.0, 37.4. These spectroscopic data are in agreement with those reported in the literature.

(R)-Dodecan-6-ol (6d)$^9$

Obtained following the general procedure (48mg, 0.24 mmol, 99%) (90:10 er); $[\alpha]_{D}^{25} -6.5$ (c. 1.0, CHCl$_3$); $\nu_{\text{max}}$ (film/cm$^{-1}$) 3320, 2956, 2923, 2853, 1467, 1377, 1351, 1137, 1071; $\delta_{\text{H}}$ (400 MHz, CDCl$_3$) 0.89-0.93 (6H, m, 2 × CH$_3$), 1.27-1.50 (18H, 9 × CH$_2$), 3.58-3.64 (1H, m, OCH); $\delta_{\text{C}}$ (100 MHz, CDCl$_3$) 14.0, 14.1, 22.6, 22.7, 25.3, 25.6, 29.4, 31.8, 31.9, 37.4, 37.5, 72.0. These spectroscopic data are in agreement with those reported in the literature.
VI. Synthesis of Epoxide 7f

(2S,3S)-2-pentyl-3-phenyloxirane (7f)

A solution of sulfido-alcohol 5f (100 mg, 0.33 mmol) was dissolved in CH₂Cl₂ (1 ml) and the solution was cooled to 0 °C. Trimethyloxonium tetrafluoroborate (488 mg, 3.30 mmol) was added and the mixture was allowed to warm to RT over 1 hr. The mixture was subsequently cooled to 0 °C and 0.5 M NaOH (4 ml) was added. The reaction was allowed to warm to RT over 24 hrs then partitioned between water and Et₂O. The aqueous layer was extracted multiple times with Et₂O and the combined organic layers were then dried over MgSO₄, filtered and evaporated to dryness. The crude oil was purified by column chromatography (Pet/EtOAc = 100/0 to 99/1) to give the epoxide as a colourless oil (34 mg, 0.18 mmol, 54%). [α]D²⁵ -13.6 (c. 1.0, CHCl₃); ν max (film/cm⁻¹) 2956, 2928, 2858, 1496, 1460, 1438, 1091, 1070, 1026, 881, 746, 700, 615; δH (400 MHz, CDCl₃) 0.93 (3H, t, J = 7.0, CH₃), 1.33-1.74 (8H, m, 4 × CH₂), 2.97 (1H, td, J = 5.6, 2.0, CHCH₂), 3.63 (1H, d, J = 2.0, PhCH), 7.27-7.39 (5H, m, 5 × ArH); δC (100 MHz, CDCl₃) 14.0, 22.6, 25.6, 31.6, 32.3, 58.7, 63.3, 125.5, 128.0, 128.4, 137.9; Found (CI): [M+H]⁺ 191.14319, C₁₃H₁₉O requires 191.14359.
VII. NMR Spectra for compounds (1 - 7)

1-(Phenylthio)-1H-1,2,4-triazole (3a)
1-Hexylsulfanyl-1,2,4-triazole (3b)
(S)-6,6-Dimethoxy-2-(phenylthio)hexan-1-ol (4a)
(S)-2-(Phenylthio)heptan-1-ol (4b)
(R)-3-Methyl-2-(phenylthio)butan-1-ol (4c)
2R,3S)-3-(Phenylthio)octan-2-ol (5a)
(1R,2S)-1-cyclohexyl-2-(phenylthio)heptan-1-ol (5b)
(1R,2S)-1-Cyclopropyl-2-(phenylthio)heptan-1-ol (5c)
(6R,7S)-7-(Phenythio)dodecan-6-ol (5d)
(5R,6S)-6-(Phenylthio)octan-5-ol (5e)
(1R,25)-1-phenyl-2-(phenylthio)heptan-1-ol (5f)
(1S,2R)-1-cyclohexyl-3-phenyl-2-(phenylthio)propan-1-ol (5g)
(1S,2R)-1-phenyl-2-(phenylthio)pent-4-en-1-ol (5h)
(1S,2R)-1-cyclohexyl-2-(phenylthio)pent-4-en-1-ol (5i)
$4R\text{-}2\text{-methyl-4-(phenylthio)hepta-1,6-dien-3-ol (5j)}$
(1S,2R)-3-methyl-1-phenyl-2-(phenylthio)butan-1-ol (5k)
(2R,3S)-3-Hexylsulfanyl-6,6-dimethoxyhexan-2-ol (5l)
(R)-Octan-2-ol (6a)
S)-1-cyclohexylheptan-1-ol (6b)
(S)-1-cyclopropylheptan-1-ol (6c)
(R)-Dodecan-6-ol (6d)
(2S,3S)-2-pentyl-3-phenyloxirane (7f)
VIII. General procedure for Mosher’s esters preparation

A solution of alcohol (1 eq.) and (S) or (R) Mosher’s acid (MTPA) (3 eq.) in CH₂Cl₂ (0.2 M) was stirred at RT. EDCI·HCl (3 eq.) was added, followed by DMAP (3.3 eq.) and the resulting solution was stirred at RT for 24 hrs. The mixture was partitioned between water and CH₂Cl₂; the phases were separated and the organic layer was dried over MgSO₄, filtered and evaporated to dryness. The crude product was analysed directly by NMR to determine the enantiopurity. In the case of the ester derived from β-hydroxysulfide 5l the ester was purified by column chromatography (Pet/EtOAc), in order to determine the absolute stereochemistry.

(S)-2(R,3S)-3-(Hexylsulfanyl)-6,6-dimethoxyhexan-2-yl-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (5l-m1)

\[
\begin{align*}
\nu_{\max} \text{ (film/cm}^{-1}) & := 2932, 2856, 1744, 1599, 1521, 1451, 1379, 1257, 1181, 1123; \\
\delta_{\ell} \text{ (400 MHz, CDCl}_3) & := 0.90 \text{ (3H, t, } J = 7.0, \text{ CH}_2CH_3), 1.24-1.38 \text{ (8H, m, (CH}_2)_3CH_3, \text{ SCHCH}_2), 1.47 \text{ (3H, d, } J = 6.3, \text{ CHCH}_3), 1.55-1.67 \text{ (3H, m, CHHCH(OMe))}, 1.88-1.97 \text{ (1H, m, CHHCH(OMe)}_2), 2.36 \text{ (1H, dt, } J = 12.1, 7.4, \text{ SCHH}), 2.43 \text{ (1H, dt, } J = 12.1, 7.4, \text{ SCHH}), 2.61 \text{ (1H, ddd, } J = 3.5, 5.3, 9.6, \text{ SCH}), 3.30 \text{ (3H, s, 3 × CH(OCH}_3)_2), 3.31 \text{ (3H, s, 3 × CH(OCH}_3)_2), 3.60 \text{ (3H, s, COCH}_3), 4.29 \text{ (3H, t, } J = 5.5, \text{ CH(OCH}_3)_2), 5.25 \text{ (1H, dq, } J = 11.9, 6.1, \text{ OCH}), 7.40-7.43 \text{ (3H, m, 3 × ArH)}, 7.56-7.58 \text{ (2H, m, 2 × ArH); } \\
\delta_{\ell} \text{ (125 MHz, CDCl}_3) & := 14.1, 17.1, 22.6, 25.9, 28.6, 29.7, 30.1, 31.4, 32.0, 50.4, 52.6, 53.0, 55.6, 84.4 \text{ (q, } J_{CF} = 28), 104.3, 123.5 \text{ (q, } J_{CF} = 290), 127.3, 128.4, 129.6, 132.5, 166.0; \\
\text{Found (TOF-MS): } [M-OMe]^+ & := 463.2111, C_{23}H_{34}O_4F_3S \text{ requires 463.2130.}
\end{align*}
\]

(R)-2(R,3S)-3-(Hexylsulfanyl)-6,6-dimethoxyhexan-2-yl-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (5l-m2)

\[
\begin{align*}
\nu_{\max} \text{ (film/cm}^{-1}) & := 2931, 2860, 1744, 1599, 1521, 1451, 1379, 1256, 1181, 1123; \\
\delta_{\ell} \text{ (400 MHz, CDCl}_3) & := 0.90 \text{ (3H, t, } J = 7.0, \text{ CH}_2CH_3), 1.24-1.43 \text{ (8H, m, (CH}_2)_3CH_3, \text{ SCHCH}_2), 1.37 \text{ (3H, d, } J = 6.3, \text{ CHCH}_3), 1.52 \text{ (1H, m, CHHCH(OCH}_3)_2), 1.65-1.75 \text{ (2H, m, SCHCH}_2), 1.94-1.98 \text{ (1H, m, CHHCH(OCH}_3)_2), 2.51 \text{ (2H, t, } J = 7.4, \text{ SCH}_2), 2.67-2.72 \text{ (1H, m, SCH), 3.32 \text{ (3H, s, 3 × CH(OCH}_3)_2), 3.33 \text{ (3H, s, 3 × CH(OCH}_3)_2), 3.58 \text{ (3H, br s, COCH}_3), 4.35 \text{ (1H, t, } J = 5.4, \text{ CH(OCH}_3)_2), 5.28 \text{ (1H,}
\end{align*}
\]
qd, \( J = 6.3, 4.7, \text{ OCH} \), 7.39-7.44 (3H, m, 3 \times \text{ Ar}H), 7.58-7.60 (2H, m, 2 \times \text{ Ar}H); \delta_C (150 \text{ MHz, CDCl}_3) 14.1, 17.3, 22.7, 25.6, 28.6, 29.7, 30.2, 31.4, 31.9, 41.4, 49.7, 51.0, 52.6, 55.6, 75.5, 80.9, 84.8 (q, \( J_{CF} = 27 \)), 104.3, 123.5 (q, \( J_{CF} = 291 \)), 127.6, 128.5, 128.7, 132.2, 166.2; Found (TOF-MS): [M-OME]^+ 463.2145, C_{23}H_{34}O_{4}F_{3}S requires 463.2130.

IX. Determination of the configuration of the secondary alcohol 5l

The Mosher’s esters analysis is based on the differences in chemical shifts of the following signals for the two diastereoisomers.

\[
\begin{array}{cccc}
\text{Proton} & \delta_S (5l-m1) & \delta_R (5l-m2) & \Delta (5l-m1, 5l-m2) \\
1 & 1.47 & 1.37 & 0.1 \\
2 & 5.25 & 5.28 & -0.03 \\
3 & 2.61 & 2.69 & -0.08 \\
\text{S-CH}_2 & 2.40 & 2.51 & -0.09 \\
6 & 4.29 & 4.35 & -0.06 \\
\end{array}
\]

From the difference in the frequencies observed above, the configuration of the secondary alcohol can be assigned as (R).
X. Determination of the enantiomeric ratios of alcohols 6a-6d.

Mosher’s Ester Analysis
Esters were prepared according to the general procedure. After extraction, the crude mixture was analysed either by $^1$H or $^{19}$F-NMR. The enantiomeric ratio was determined from the integration of the peaks of the two diastereoisomers (peaks expanded in the NMR spectra).

Calculation of Enantiomeric Ratio
Assuming that no racemisation occurs during the reaction, addition of the Grignard reagent (R$_1$-MgX) to enantiomerically the enriched $\alpha$-sulfidoaldehyde (e.g. using the er of alcohol 1b, measured as 94:6) should give four stereoisomers as shown below, which, based on the dr for 5b (98:2) observed by $^1$H-NMR, would be in a 94.1:3.9:1.9:0.1 ratio (The diastereoisomers of the b-hydroxysulfides were typically inseparable). After removal of the sulfide substituent by Raney-Ni reduction, and therefore removal of one chiral centre, the ratio between the two enantiomers of alcohol 6b can be calculated as the ratio between the sums of the ratios of enantiomer R and enantiomer S derived from the corresponding diastereoisomers of sulfido-alcohols 5b (approximately 92:8).
Calculated enantiomeric ratios for alcohols 6a-6d

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>er of alcohol 4</th>
<th>dr of alcohol 5</th>
<th>Calculated er of 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>6a</td>
<td>94:6</td>
<td>91:9</td>
<td>87:13</td>
</tr>
<tr>
<td>6b</td>
<td>94:6</td>
<td>98:2</td>
<td>92:8</td>
</tr>
<tr>
<td>6c</td>
<td>94:6</td>
<td>93:7</td>
<td>88:12</td>
</tr>
<tr>
<td>6d</td>
<td>94:6</td>
<td>97:3</td>
<td>91:9</td>
</tr>
</tbody>
</table>
Determination of the er of alcohol 4a (96:4 er)
Determination of the er of alcohol 4b (98:2 er)
Determination of the er of alcohol 4c (99:1 er)

![Diagram of molecular structures 4c-m1 and 4c-m2 with corresponding ppm values.](image-url)
Determination of the er of alcohol 6a (84:16er)
Determination of the er of alcohol 6b (92:8 er)
Determination of the er of alcohol 6c (88:12 er)

\[ \text{Diagram of molecules 5b-m1 and 5b-m2} \]
XI. References