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A new and efficient route to homochiral γ-hydroxysulfoxides and γ-hydroxysulfones

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Abstract—Readily available (+)-(*R*)-1,3-diphenyl-3-phenylsulfanyl-propan-1-one **1** was oxidized to the corresponding sulfone and its reduction gave separable (1*R*,3*R*)- and (1*S*,3*R*)-1,3-diphenyl-3-phenylsulfonylpropan-1-ols. When **1** was reduced to the mixture of epimeric alcohols, subsequent reaction with three different sulfoxidation agents allowed the separation of all four diastereomeric 1,3-diphenyl-3-phenylsulfinylpropan-1-ols in diastereomerically pure form. The absolute configuration at the newly created stereogenic carbon was proved by chemical correlation, while the configuration of the sulfur centre of the phenylsulfinyl group was established by CD spectroscopy.

1. Introduction

Hydroxysulfoxides constitute an important class of chiral building blocks. Usually, their preparation is based on the diastereoselective reduction of the corresponding ketosulfoxides. This method is particularly suitable for the preparation of β-hydroxysulfoxides of the required configuration.[1] In a few cases the same approach has also been applied to obtain the respective γ-hydroxy derivatives.[2] Recently, we have described a facile and enantioselective method for the multigram preparation of the Michael adducts via addition of thiophenols to chalcones.[3] The thus obtained optically active γ-ketosulfides possess two prostereogenic centers, suitable for further transformation into hydroxy-, sulfinyl- or sulfonyl functionalities. Since we are interested in the preparation of stereodifferentiating ligands, we undertook the elaboration of both prochiral groups into new chiral derivatives of this type, with divergent stereochemistry.

Herein we report a simple, two-step transformation of the Michael adduct into γ-hydroxysulfoxides and γ-hydroxysulfones, interesting chiral building blocks with three or two stereogenic centers, respectively. We also describe their further conversions into enantiomeric alcohols and cyclopropane derivatives.

2. Results and discussion

Reduction of (+)-(*R*)-1,3-diphenyl-3-phenylsulfanyl-propan-1-one **1**[3] with lithium aluminum hydride (LAH) led to an inseparable mixture of diastereomeric alcohols **2** in excellent yield but with d.r. of ca. 1:1. Application of other reducing agents, namely DIBAL-H, DIBAL-H/$ZnCl_2$ or $NaBH_4$ was ineffective. However, when (*R*)-**1** was oxidized with Oxone® to the corresponding sulfone (*R*)-**3**, its subsequent reduction with LAH also gave a mixture of diastereomers (24% de). Fortunately, in this case both products (*R*,*R*)- and (*R*,*S*)-**4** could be separated completely by crystallization. The pure diastereomer obtained, (*R*,*S*)-**4**, was desulfonylated to afford the known (*S*)-1,3-diphenylpropanol-1 **5**.[4] Alcohol (*R*,*S*)-**4** was mesylated to give (*R*,*S*)-**6**, which reacted in the presence of potassium *tert*-butoxide and a catalytic amount of 18-crown-6 via intramolecular S_N2 reaction[5] resulting in homochiral (*E*)-1,2-diphenyl-1-phenylsulfonylcyclopropane **7** (Scheme 1). Here, the stereochemical assignment is based on the fact that a single optically active diastereomer with *cis*-located phenyl groups (see: NOESY correlations, 500 MHz) was obtained as the only product. Unfortunately, desulfonylation[6] of **7** furnished the mixture of *cis*- and *trans*-1,2-diphenylcyclopropane and no stereoselective method for this transformation was found.

In order to exploit the well known stereodirecting properties of the phenylsulfinyl group,[1] we attempted diastereoselective sulfoxidation of the adduct **1**. How-

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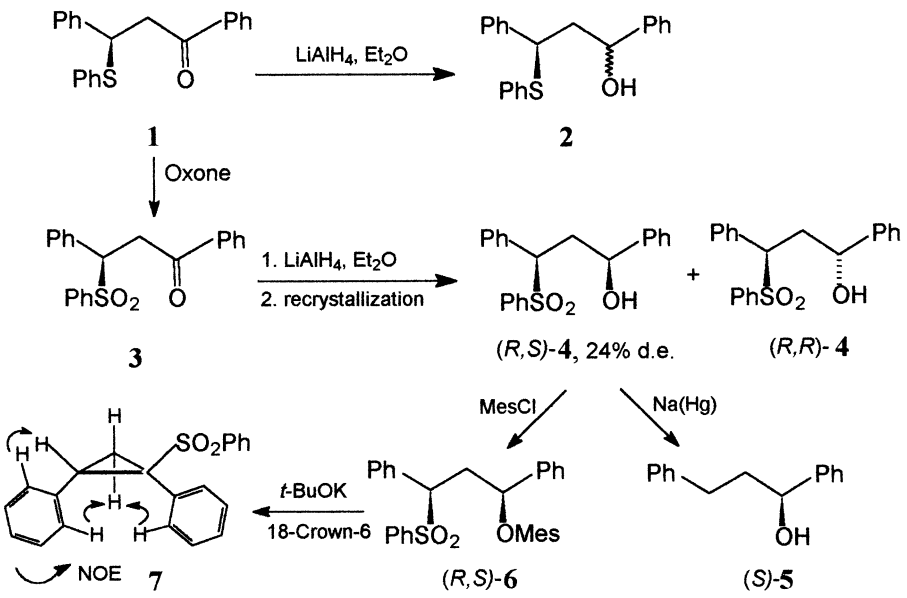
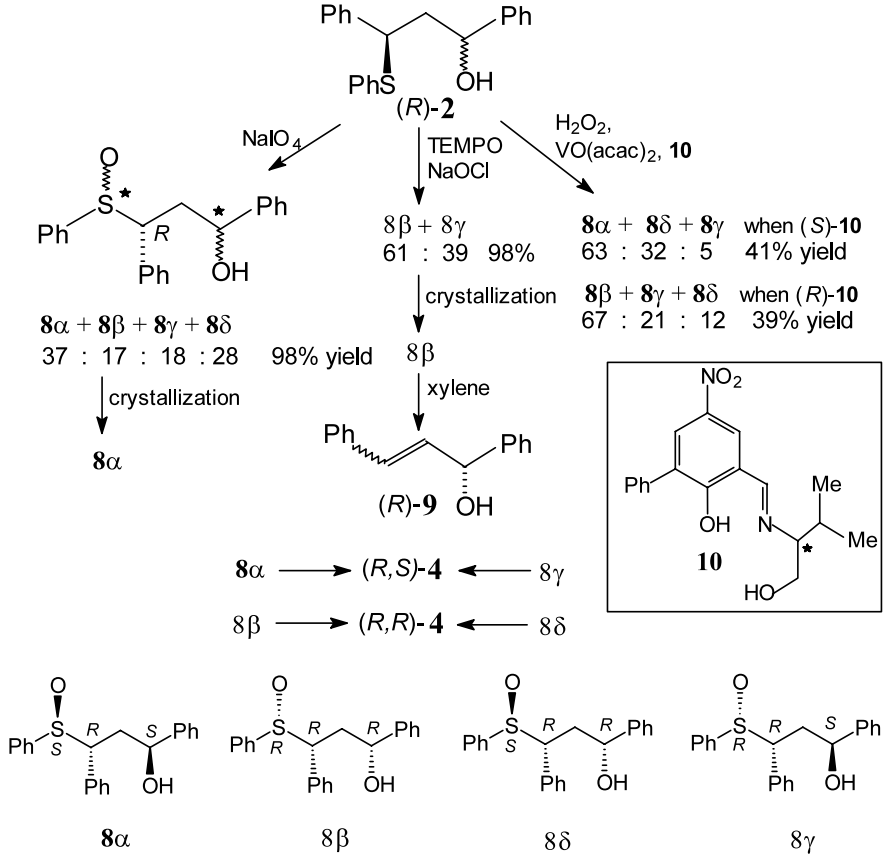


Scheme 1.

ever, the substrate did not react with mild oxidants (see below) and ultimately the use of MCPBA resulted in retro-Michael reaction and chalcone was isolated in 46% yield. We therefore attempted sulfoxidation of the reduced adduct, i.e. diastereomeric mixture of (*R*)-**2**. When a mild chemoselective oxidant ($NaIO_4$)[7] was used, all four possible diastereomeric γ-hydroxysulfoxides **8** (**α**,**β**,**γ**,**δ**) were formed in comparable yields (Scheme 2). The ^1H NMR spectrum for each diastereomer was different from the others in the resonance pattern for the methine hydrogens (3.5–5.5 ppm). Recrystallization of the mixture gave a single diastereomerically pure isomer **8α** in 21% yield. Further oxidation of this product with Oxone®[8] produced the



Scheme 2.

sulfone with identical physical and spectroscopic properties to (*R*,*S*)-**4**.

The diastereoselective catalytic TEMPO/sodium hypochlorite system,[9] was then applied. Only two diastereomers of **8** (**β** and **γ**) were produced, both different from the previously isolated one. The main diastereomer **8β** (22% de) crystallized readily in pure form. The second one (**8γ**) was isolated by chromatography and recrystallization after stereoselective sulfoxidation (see below). Both the major **8β** and minor **8γ** were oxidized with Oxone® to (*R*,*R*)-**4** and (*R*,*S*)-**4**, respectively. Moreover, on boiling in xylene **8β** underwent thermal elimination furnishing a *cis*/*trans* mixture of the known (+)-(*R*)-allylic alcohol **9**.[10] At this point of the study the absolute configuration at the sulfur atom in all of the obtained γ-hydroxysulfoxides remained unknown.

In order to solve this problem we used our optimized version (30% H_2O_2/$VO(acac)_2$-chiral ligand **10**)[11] of the Bolm catalytic sulfoxidizing system.[12] The system, when containing (*S*)-ligand **10**, is known for the preferred formation of sulfoxides with S_S configuration and with (*R*)-**10**, R_S configuration.[11,12] Thus, when the oxidant containing ligand (*S*)-**10** was applied, three diastereomers were detected by ^{1}H NMR, with two of them (**8α** and **8δ**) dominating. Fortunately, again all of the diastereomers of **8** were separable, one of which was identical with that previously isolated after oxidation with $NaIO_4$, i.e. **8α** (26% yield). Based on this, we tentatively assigned the stereochemistry as (*R*,*S*,S_S)-**8**. In the next experiment we used (*R*)-**10** and the main formed product (**8β**, 26% yield) was identical with the major product obtained after oxidation with TEMPO/NaOCl. On these grounds we assigned it as (*R*,*R*,R_S)-**8**. In the same way we provisionally assigned the absolute configuration of both remaining sulfoxides; **8δ** being (*R*,*R*,S_S)-**8** and **8γ** being (*R*,*S*,R_S)-**8**. In order to verify our assignments of absolute configuration at the stereogenic sulfur centre we studied the CD spectra of the obtained γ-hydroxysulfoxides **8** and, for comparison their oxidation products (*R*,*R*)-**4** and (*R*,*S*)-**4**.

It has long been known that the absolute configuration of sulfoxides correlates with their chiroptical properties.[13] The phenylsulfinyl group was considered by Mislow as an inherently chiral chromophore where the sign of the Cotton effects (CE) is determined solely by the absolute configuration of the chromophore.[13a] Its primary UV band (σ→σ*, S–O, usually at 235–255 nm, log ε ca. 3.6) is optically active with a CE, Δε of ca. 20. Additionally, the shorter wavelength absorption (^1L_a, phenyl ring, ca. 220 nm, log ε ca. 4.1) demonstrates a CE of similar amplitude but of opposite sign. For the phenylsulfinyl group, a negative CE for the primary band corresponds to (*S*)-configuration.[9b,13] This correlation has recently been ascribed to the coupling of the transition dipole moments for both bands, which defines the chirality.[14] We measured the UV and CD spectra of all our diastereomeric sulfoxides and sulfones. The results are shown in Table 1 and Figs. 1 and 2. In the absence of the stereogenic sulfur centre (sulfone **4**), disregarding the presence of the stereogenic carbon atoms, the long wavelength UV band disappears, so the CD curve does not show any chirality in this range (Δε=0 for λ>240 nm) (Figs. 1 and 2). Even in the presence of an additional UV-absorbing group the CD curves for diastereomers differing in configuration at the stereogenic sulfur were almost mirror images. We have already observed similar feature for β-aminosulfoxides.[9b] The results collected in Table 1 allows unambiguous assignment of configuration at the newly created sulfur stereocenters. Thus our provisional assignments were correct, as is confirmed by the data in Table 1.

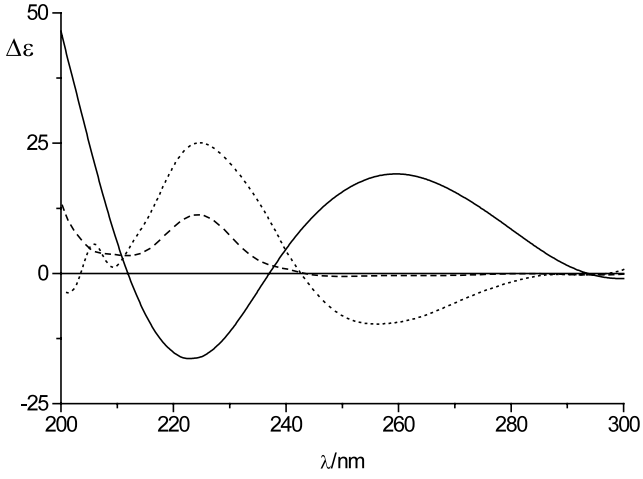


Figure 1. CD spectra of (1*S*,3*R*,R_S)-**8** (solid line), (1*S*,3*R*,S_S)-**8** (dotted line) and (1*S*,3*R*)-**4** (dashed line) in acetonitrile solution.

Table 1. UV and CD spectra[a]

Compound	UV absorption properties	Circular dichroism		
	λ_{max} (10^{-3} ε)	λ (Δε)	λ (0)	λ (Δε)
(1*R*,3*R*,R_S)-**8**	216 (16.8), 258 (5.97)	226 (−36.6)	241	258 (20.6)
(1*S*,3*R*,S_S)-**8**	216 (18.0), 256 (5.83)	225 (25.1)	243	256 (−9.7)
(1*S*,3*R*,R_S)-**8**	216 (13.3), 258 (3.50)	223 (−16.3)	237	260 (19.1)
(1*R*,3*R*,S_S)-**8**	216 (19.9), 256 (6.81)	226 (44.8)	244	258 (−17.8)
(1*S*,3*R*)-**4**	218 (16.4)			
(1*R*,3*R*)-**4**	216 (16.0)			

[a] Spectra were recorded in acetonitrile at the concentration range of 10^{-4}–10^{-5} M.

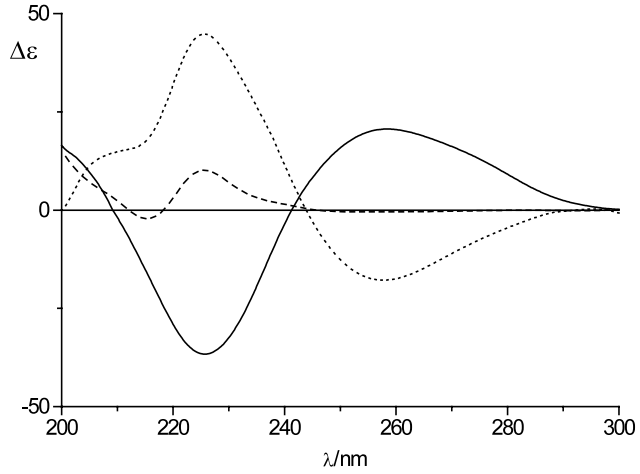


Figure 2. CD spectra of (1*R*,3*R*,R_S)-**8** (solid line), (1*R*,3*R*,S_S)-**8** (dotted line) and (1*R*,3*R*)-**4** (dashed line) in acetonitrile solution.

3. Conclusions

The readily available adduct of thiophenol to chalcone allows, after oxidation to the sulfone and subsequent reduction of the ketone function, easy separation of the respective diastereomeric alcohols. These derivatives are suitable for further transformations. Chemo- and stereoselective sulfoxidations of epimeric γ-hydroxysulfides gave, after recrystallization, all four diastereomeric γ-hydroxysulfoxides in diastereomerically pure form. Thus, sequential reduction and oxidation of the two prochiral groups of the enantiomeric precursor allows simple preparation of all possible products with three stereogenic centers.

4. Experimental

4.1. General

Melting points were determined using a Boetius hot-stage apparatus and are uncorrected. IR spectra were recorded on a Perkin–Elmer 1600 FTIR spectrophotometer. ^{1}H and ^{13}C NMR spectra were measured on a Bruker CPX (^{1}H, 300 MHz) or a Bruker Avance (^{1}H, 500 MHz) spectrometer using TMS as an internal standard. UV and CD spectra were recorded for CH_3CN solutions using a Hewlett–Packard 8452 diode array spectrophotometer and a JASCO J 600 spectropolarimeter, respectively. Observed rotations at 589 nm were measured using an Optical Activity Ltd. Model AA-5 automatic polarimeter. GC–MS analyses were determined on a Hewlett–Packard 5890 II gas chromatograph (25 m capillary column) with a Hewlett–Packard mass spectrometer 5971 A operating on the electron impact mode (70 eV). Separations of products by chromatography were performed on silica gel 60 (230–400 mesh) purchased from Merck. Thin-layer chromatography analyses were performed using silica gel 60 precoated plates (Merck).

4.2. (*R*)-1,3-Diphenyl-3-phenylsulfanylpropan-1-one 1

Compound **1** was prepared as described previously.[3]

4.3. General procedure for reductions with $LiAlH_4$

To a suspension of lithium aluminum hydride (0.34 g, 9 mmol) in absolute ether (250 ml), ketone **1** or **3** (7 mmol) was added gradually. The resulting mixture was heated under reflux for 3 h. Then, ether saturated with water (30 ml), H_2O (10 ml), and 15% aqueous sodium hydroxide (ca. 20 ml) were subsequently introduced to the cooled solution. After 30 min of stirring, the organic layer was separated from the granulated precipitate, and the solid was washed twice with ether (30 ml). The combined ethereal extract was dried over K_2CO_3 and evaporated. The products obtained were analytically pure: **2** (inseparable 1:1 diastereomeric mixture), and **4** (separated by recrystallization from methylene dichloride–*n*-hexane).

4.3.1. (3*R*)-1,3-Diphenyl-3-phenylsulfanylpropan-1-ol, 2: (diastereomeric ratio 1:1). Yield 98%; Oil, ^{1}H NMR ($CDCl_3$): 1.76 (br s, 1H, OH), 2.13–2.24 and 2.25–2.36 (two m, 2H, CH_2), 4.15 and 4.33 (t, $J=7.4$ Hz, dd, $J_1=9.8$ Hz, $J_2=5.6$ Hz, 1H, S-CH), 4.44 and 4.78 (dd, $J_1=9.3$ Hz, $J_2=3.6$ Hz, dd, $J_1=7.6$ Hz, $J_2=5.9$ Hz, 1H, CH), 7.08–7.25 (m, 15H, ArH); IR (film): 3410, 3060, 1583, 1493, 1453, 1054, 1025, 747, 699 cm^{-1}; MS (EI, 70 eV): m/z (%)=320 (1) [M$^+$], 210 (51), 110 (55), 107 (91), 79 (100), 77 (90), 65 (31), 51 (31); $[\alpha]_D^{20}=+142$ (1.38, CH_2Cl_2); $R_f=0.43$ (*tert*-BuOMe/$CHCl_3$/hexane, 2.0:2.0:7.0). These characteristics are in general agreement with the literature data for the racemic mixture of diastereomers.[15]

4.3.2. 1,3-Diphenyl-3-phenylsulfonylpropan-1-ol, 4. Yield >95%. D.e.=24% (62:38). The diastereomers were separated by several recrystallizations from CH_2Cl_2/hexane; the major (1*S*,3*R*)-**4** crystallizes, while the minor (1*R*,3*R*)-**4** is retained in the mother liquor.

4.3.2.1. (+)-(1*S*,3*R*)-4. Mp=191–192°C (CH_2Cl_2/hexane); $[\alpha]_D^{20}=+77$ (0.20, CH_2Cl_2, >95% ee); ^{1}H NMR ($CDCl_3$), δ: 1.76 (br s, 1H, OH), 2.35–2.44 (m, 1H, CH_2), 2.67–2.77 (m, 1H, CH_2), 4.32 (d, 1H, $J=9.0$ Hz, CH), 4.48 (dd, 1H, $J_1=11.4$ Hz, $J_2=4.5$ Hz, CH), 7.09–7.12 (m, 2H, ArH), 7.18–7.32 (m, 10H, ArH), 7.44–7.46 (m, 3H, ArH); ^{13}C NMR ($CDCl_3$), δ: 36.8 (CH_2), 68.6 ($\underline{C}HSO_2Ph$), 70.8 ($\underline{C}HOH$), 125.6, 128.0, 128.6, 128.7, 128.9, 129.0, 130.1, 132.0, 133.4, 137.4, 143.7; IR (KBr): 3464, 3058, 1494, 1447; 1289, 1143, 1067, 749, 701, 561 cm^{-1}. Anal. calcd for $C_{21}H_{20}SO_3$ (M=352.391): C, 71.51; H, 5.72; S, 9.08. Found: C, 71.78; H, 5.67; S, 9.07%.

4.3.2.2. (+)-(1*R*,3*R*)-4. Mp=108–110°C (CH_2Cl_2/hexane); $[\alpha]_D^{20}=+59$ (0.96, CH_2Cl_2, >95% ee); ^{1}H NMR ($CDCl_3$) δ: 2.13 (br s, 1H, OH), 2.54–2.63 (m, 1H, CH_2), 2.81–2.90 (m, 1H, CH_2), 4.02–4.06 (m, 1H, CH), 4.77–4.81 (m, 1H, CH), 7.02 (d, 2H, $J=7.3$ Hz, ArH), 7.21–7.36 (m, 10H, ArH), 7.43–7.55 (m, 3H, ArH); ^{13}C NMR ($CDCl_3$) δ: 37.5 (CH_2), 68.1 ($\underline{C}HSO_2Ph$), 72.0

(CHOH), 126.1, 128.2, 128.5, 128.6, 128.7, 128.8, 128.9, 129.0, 129.9, 132.7, 133.5, 142.7; IR (KBr): 3555, 3027, 1492, 1448, 1298, 1290, 1142, 1086, 1053, 701, 692, 594 cm^{-1}.

4.4. Representative procedure for preparation of sulfones

A solution of sulfide **1** (1 mmol) in methanol (20 ml) was treated with Oxone® (2.2 mmol, 1.35 g) in water (20 ml) (in the case of oxidation of 1 mmol of sulfoxides **8**, 1.1 mmol of oxidant was used). The reaction mixture was stirred at room temperature for 2 h. The solution was extracted with CH_2Cl_2 (30 ml), the organic phase was separated, dried over Na_2SO_4, and evaporated under reduced pressure. The products were recrystallized or chromatographed on silica gel.

4.4.1. (+)-(*R*)-1,3-Diphenyl-3-phenylsulfonylpropan-1-one, 3. Yield >95%. Mp = 159–160°C (MeOH); lit.[16] (rac) mp = 159°C (EtOH), 155.1°C (MeOH); $[\alpha]_D^{20}$ = +141 (1.13, CH_2Cl_2, >95% ee); ^1H NMR ($CDCl_3$): δ = 3.79–3.88 (m, 1H, CH_2), 3.99–4.07 (m, 1H, CH_2), 4.83 (dd, 1H, J_1 = 9.6 Hz, J_2 = 4.8 Hz, CH), 7.08–7.15 (m, 5H, ArH), 7.25–7.38 (m, 4H, ArH), 7.43–7.50 (m, 4H, ArH), 7.83 (m, 2H, ArH); ^{13}C NMR ($CDCl_3$), δ: 37.3 (CH_2), 66.9 (CHSO$_2$Ph), 128.1, 128.4, 128.7, 128.7, 128.8, 128.9, 129.7, 132.5, 133.7, 133.7, 136.1, 136.9, 194.8 (C=O); IR (KBr): 3064, 1687, 1674, 1597, 1448, 1306, 1232, 1145, 1084, 986, 753, 689, 560 cm^{-1}. Anal. calcd for $C_{12}H_{18}O_3S$ (M = 350.375): C, 71.98; H, 5.17; S, 9.13. Found: C, 71.73; H, 5.29; S, 9.16%.

4.5. Desulfonylation

The reaction of sulfones (1*S*,3*R*)-**4** and **7** with 6% sodium amalgam was run in methanol according to a standard procedure.[17]

4.5.1. (−)-(*S*)-1,3-diphenylpropan-1-ol, 5. Yield 86%. Mp = 44–46°C; $[\alpha]_D^{20}$ = −14.5 (1.0, MeOH, >90% ee); lit.[4a] $[\alpha]_D^{20}$ = +16.2 (1.17, MeOH, 96% ee) for (*R*)-**5**, lit.[4b] $[\alpha]_D^{20}$ = −14.8 (0.5, MeOH, >99% ee) for (*S*)-**5**; ^1H NMR ($CDCl_3$) δ: 1.79 (s, 1H, OH), 2.04–2.16 (m, 2H, CH_2), 2.67–2.77 (m, 2H, CH_2), 4.69 (dd, 1H, J_1 = 7.4 Hz, J_2 = 5.7 Hz, CH), 7.19–7.36 (m, 10H, 2×ArH); IR (KBr): 3395, 3027, 2940, 1603, 1495, 1454, 1058, 747, 699 cm^{-1}. MS (EI, 70 eV): m/z (%) = 212 (6) [M^+], 194 (38) [212-OH], 107 (100) [PhCHOH$^+$].

4.6. Representative procedure for mesylation

A round-bottomed flask cooled in an ice bath was charged with alcohol (1*S*,3*R*)-**4** (0.35 g, 1 mmol), toluene (30 ml) and triethylamine (0.56 ml, 4 mmol). Methanesulfonyl chloride (0.10 ml, 1.3 mmol) was then added with a syringe. The mixture was stirred at 5°C overnight. The reaction was quenched with water (10 ml), the product was extracted with ether (20 ml), and the organic layer was subsequently washed with 1 M aqueous HCl (15 ml), water (10 ml), satd $NaHCO_3$ solution (10 ml), brine (10 ml) and dried with sodium sulfate. After solvent evaporation the product (1*S*,3*R*)-**6** was recrystallized from ethanol.

4.6.1. (+)-(1*S*,3*R*)-(1,3-Diphenyl-3-phenylsulfonylpropyl) methanesulfonate, 6. Yield 86%, de 100%. Mp = 81–83°C (EtOH); $[\alpha]_D^{20}$ = +50 (0.51, CH_2Cl_2, >95% ee); ^1H NMR ($CDCl_3$) δ: 2.49 (s, 3H, CH_3), 2.57–2.58 (m, 1H, CH_2), 3.11–3.15 (m, 1H, CH_2), 4.34–4.39 (dd, 1H, J_1 = 11.6 Hz, J_2 = 2.9 Hz, CH), 5.16–5.19 (dd, 1H, J_1 = 10.7 Hz, J_2 = 2.2 Hz, CH), 7.11–7.50 (m, 15H, ArH); ^{13}C NMR ($CDCl_3$) δ: 35.1 (CH_2), 39.2 (CH_3), 67.9 (CHSO$_2$Ph), 81.1 (CHSO$_3$Me), 126.7, 128.7, 128.8, 129.0, 129.1, 129.3, 129.7, 130.1, 131.0, 133.7, 136.9, 137.3; IR (KBr): 3017, 1448, 1360, 1306, 1172, 1146, 894, 699, 574 cm^{-1}.

4.7. Representative procedure for cyclopropanation

Potassium *tert*-butoxide (0.04 g, 0.35 mmol), 18-Crown-6 (7.13 mg, 0.027 mmol), dry toluene (10 ml) and (1*S*,3*R*)-**6** (0.12 g, 0.27 mmol) were introduced into a round-bottomed flask. The resulting solution was stirred at room temperature for 8 h, then ice-cold water (15 ml) was added, and the mixture was extracted with ether (20 ml). The organic layer was separated, washed with 1 M aqueous HCl (15 ml), water (10 ml), brine (10 ml) and dried over Na_2SO_4. After solvent evaporation the crude product (*E*)-**7** was recrystallized from methylene dichloride/hexane.

4.7.1. (−)-(1*R*,2*R*)-1,2-Diphenyl-1-phenylsulfonylcyclopropane, 7. Yield >95%. Mp = 181–182.5°C (CH_2Cl_2/hexane); lit.[18] (rac) mp = 211–212°C; $[\alpha]_D^{20}$ = −141 (0.6, CH_2Cl_2, >95% ee); ^1H NMR ($CDCl_3$) δ: 1.82 (dd, 1H, H_{3a}), 2.38 (dd, 1H, H_{3b}), 3.58 (dd, 1H, H_2), 6.76–6.79 (m, 4H, Ph_1, Ph_2, *o*-H), 7.00 (t, 2H, Ph_1, *m*-H), 7.06–7.08 (m, 3H, Ph_2, *m*-H, *p*-H), 7.14 (t, 1H, Ph_1, *p*-H), 7.38 (t, 2H, $PhSO_2$, *m*-H), 7.48 (d, 2H, $PhSO_2$, *o*-H), 7.55 (t, 1H, $PhSO_2$, *p*-H); ^{13}C NMR ($CDCl_3$, 500 MHz) δ: 18.2 (C_2), 28.5 (C_3), 54.5 (C_1), 127.2 (Ph_2, $C_{4'}$), 128.1, 128.3, 128.4, 128.9; 129.4 (SO_2Ph, $C_{2'}$, $C_{6'}$), 130.2 (Ph_1, $C_{1'}$), 133.7 (SO_2Ph, $C_{4'}$), 133.8 (Ph_1, $C_{2'}$, $C_{6'}$), 135.3 (Ph_2, $C_{1'}$), 138.3 (SO_2Ph, $C_{1'}$); IR (KBr): 3060, 3027, 1497, 1446, 1309, 1148, 817, 697, 688, 601, 562 cm^{-1}. Anal. calcd for $C_{21}H_{18}O_2S$ (M = 334.43): C, 75.41; H, 5.42; S, 9.57. Found: C, 75.28; H, 5.64; S, 9.60%.

4.8. Representative procedures for oxidation of sulfides

4.8.1. Oxidation with sodium periodate. A solution of $NaIO_4$ (0.206 g, 0.96 mmol) in water (1.5 ml) was added to hydroxysulfide **2** (0.238 g, 0.74 mmol) dissolved in acetone (6 ml). The reaction mixture was stirred at rt for 2 h and extracted with CH_2Cl_2 (2×15 ml). The combined organic phase was dried with Na_2SO_4, evaporated to dryness, analyzed by NMR and recrystallized from toluene to give (1*S*,3*R*,S_S)-**8**.

4.8.2. General procedure for oxidation with NaOCl/TEMPO. A 50 ml flask was charged with a solution of sulfide **2** (3 mmol) in CH_2Cl_2 (20 ml), TEMPO (0.09 mmol, 14 mg), and saturated aqueous solution of $NaHCO_3$ (16 ml) containing KBr (36 mg, 0.3 mmol). To this cooled (0°C, ice-water bath) and well-stirred mixture a solution of NaOCl (0.90 M, 3.6 ml) in saturated $NaHCO_3$ (4 ml) was added dropwise. The

mixture was stirred for 2 h at 0°C (monitored by TLC) and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (3×10 ml) and the combined organic phase was washed with water, brine and dried (Na_2SO_4). Solvent was evaporated, the crude product was analyzed by NMR and pure (1*R*,3*R*,R_S)-**8** crystallized from toluene.

4.8.3. Oxidation with H_2O_2, $VO(acac)_2$ and chiral Schiff base. Vanadyl acetylacetonate (5.2 mg, 0.02 mmol) and ligand **10**[11b] (0.03 mmol) were dissolved in a test tube in dichloromethane (4 ml), and the solution was stirred for 5 min at 25°C. After the addition of the sulfide **2** (2 mmol) the solution was cooled to 0°C and 30% H_2O_2 (0.26 ml, 2.3 mmol) was added dropwise during 10 min. The mixture was stirred for 20 h at 0°C and extracted with CH_2Cl_2 (2×5 ml). The combined organic extracts were washed with H_2O, brine and dried over Na_2SO_4. The solvent was removed in vacuo and the crude product analyzed by NMR was chromatographed on silica gel (*t*-BuOMe/$CHCl_3$/hexane) and the collected fractions were recrystallized from methylene dichloride/hexane to give in each case three pure diastereomers (see: Scheme 2).

4.8.4. 1,3-Diphenyl-3-phenylsulfinylpropan-1-ol, 8

4.8.4.1. (1*R*,3*R*,R_S)-8. Mp = 130–132°C (toluene). $[\alpha]_D^{20}$ = +126 (0.7, CH_2Cl_2); ^{1}H NMR ($CDCl_3$), δ: 2.41–2.50 (m, 1H, CH_2), 2.64–2.73 (m, 1H, CH_2), 2.74 (s, 1H, OH), 3.88 (t, 1H, J = 7.2 Hz, CH-S), 4.97 (t, 1H, J = 6.3 Hz, CH-O), 6.82 (d, 2H, J = 7.3 Hz, ArH), 7.06 (d, 2H, J = 7.4 Hz, ArH), 7.15–7.40 (m, 11H, ArH); ^{13}C NMR ($CDCl_3$), δ: 37.3, 66.5, 71.6, 125.1, 126.1, 128.0, 128.0, 128.3, 128.4, 128.7, 129.4, 130.9, 132.2, 140.2, 143.4; IR (KBr): 3363, 3085, 3057, 3028, 2909, 1494, 1447, 1024, 1017, 989, 747, 699 cm^{-1}. Anal. calcd for $C_{21}H_{20}O_2S$ (M = 336.434): C, 74.96; H, 5.99; S, 9.53. Found: C, 74.71; H, 6.09; S, 9.40%.

4.8.4.2. (1*S*,3*R*,R_S)-8. Mp = 140–141.5°C (CH_2Cl_2/hexane); $[\alpha]_D^{20}$ = +53 (0.2, CH_2Cl_2); ^{1}H NMR ($CDCl_3$), δ: 1.74 (s, 1H, OH), 2.42– 2.49 (m, 1H, CH_2), 2.59–2.66 (m, 1H, CH_2), 4.23 (dd, 1H, J_1 = 9.9 Hz, J_2 = 4.8 Hz, CH-S), 4.57 (d, 1H, J = 9.5 Hz, CH-O), 6.91 (d, 2H, J = 7.0 Hz, ArH), 7.05 (d, 2H, J = 7.0 Hz, ArH), 7.14–7.36 (m, 11H, ArH); ^{13}C NMR ($CDCl_3$), δ: 38.5, 67.5, 72.1, 125.1, 125.8, 127.2, 127.8, 128.1, 128.3, 128.6, 128.7, 129.5, 130.9, 137.5, 144.2; IR (KBr): 3374, 3059, 3026, 2918, 1494, 1445, 1016, 995, 747, 699 cm^{-1}.

4.8.4.3. (1*S*,3*R*,S_S)-8. Mp = 145–148°C (toluene); $[\alpha]_D^{20}$ = +65 (0.75, CH_2Cl_2); ^{1}H NMR ($CDCl_3$), δ: 2.38–2.45 (m, 1H, CH_2), 2.72–2.80 (m, 1H, CH_2), 2.95 (br s, 1H, OH), 4.16 (dd, 1H, J_1 = 8.8 Hz, J_2 = 4.9 Hz, CH-S), 4.56 (d, 1H, J = 8.9 Hz, CH-O), 6.97 (d, 2H, J = 6.4 Hz, ArH), 7.20–7.41 (m, 13H, ArH); ^{13}C NMR ($CDCl_3$), δ: 40.1, 70.7, 71.6, 125.2, 125.7, 127.7, 128.3, 128.6, 128.6, 128.8, 129.3, 131.3, 134.0, 141.7, 144.4; IR (KBr): 3296, 3063, 3024, 2913, 1494, 1454, 1444, 1086, 1066, 1032, 748, 698 cm^{-1}.

4.8.4.4. (1*R*,3*R*,S_S)-8. Mp = 111–113°C (CH_2Cl_2/ hexane); $[\alpha]_D^{20}$ = +97 (0.6, CH_2Cl_2); ^{1}H NMR ($CDCl_3$), δ: 2.54–2.63 (m, 1H, CH_2), 2.81–2.87 (m, 1H, CH_2), 2.91 (s, 1H, OH), 3.72 (t, 1H, J = 5.9 Hz, CH-S), 4.86 (t, 1H, J = 4.8 Hz, CH-O), 6.84 (d, 2H, J = 6.8 Hz, ArH), 7.12–7.35 (m, 13H, ArH); ^{13}C NMR ($CDCl_3$), δ: 39.9, 69.8, 72.1, 125.5, 126.5, 128.2, 128.8, 128.9, 128.9, 129.0, 129.5, 131.6, 134.5, 142.0, 143.6; IR (KBr): 3400, 3059, 3031, 2921, 2890, 1451, 1445, 1055, 1036, 1021, 759, 750, 698 cm^{-1}.

4.9. Representative procedure for elimination reaction

Hydroxysulfoxide (1*R*,3*R*,R_S)-**8** (70 mg, 0.21 mmol) was dissolved in xylene (1.5 ml) and anhydrous Na_2CO_3 was added in excess. The mixture was heated under reflux for 1 h (monitored by TLC). The solvent was evaporated. The residue was dissolved in CH_2Cl_2, washed with water and brine and dried (Na_2SO_4). Product **9** was purified by column chromatography.

4.9.1. (+)-(*R*)-3-Hydroxy-1,3-diphenylprop-1-ene, 9. Yield 87%. 6:4 *trans*/*cis* mixture; $[\alpha]_D^{20}$ = +20.3 (0.74, CH_2Cl_2); lit.[10] $[\alpha]_D^{20}$ = +28.1 (1, CH_2Cl_2) for *trans*-(+)-(*R*)-**9**, ^{1}H NMR ($CDCl_3$), δ: 1.86 (br s, 1H, OH), 5.10 (t, 0.4H, J = 6.36 Hz CH-O, *cis*-isomer) 5.38 (d, 0.6H, J = 6.4 Hz, CH-O, *trans*-isomer), 6.38 (two dd, 1H, J_1 = 15.9 Hz, J_2 = 6.4 Hz, CH), 6.68 (d, 1H, J = 15.9 Hz, CH), 7.22–7.44 (m, 10H, ArH).

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References

1. (a) Mikołajczyk, M.; Drabowicz, J.; Kiełbasiński, P. *Chiral Sulfur Reagents. Applications in Asymmetric and Stereoselective Synthesis*; CRC Press: Boca Raton, 1997; (b) Carreño, M. C. *Chem. Rev.* **1995**, *95*, 1717–1760; (c) *Organosulfur Chemistry*; Page, P. C. B., Ed.; Academic Press: San Diego/London, 1998; Vol. 2.
2. (a) Arai, Y.; Suzuki, A.; Masuda, T.; Masaki, Y.; Shiro, M. *Chem. Pharm. Bull. Jpn.* **1996**, *44*, 1765–1769; (b) Solladie, G.; Colobert, F.; Sommy, F. *Tetrahedron Lett.* **1999**, *40*, 1227–1228; (c) Nakamura, S.; Kuroyanagi, M.; Watanabe, Y.; Toru, T. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3143–3148; (d) Nakamura, S.; Oda, S.; Yasuda, H.; Toru, T. *Tetrahedron* **2001**, *57*, 8469–8480.
3. Skarżewski, J.; Zielinska-Błajet, M.; Turowska-Tyrk, I. *Tetrahedron: Asymmetry* **2001**, *12*, 1923–1928.
4. (a) Node, M.; Nishide, K.; Shigeta, Y.; Shiraki, H.; Obata, K. *J. Am. Chem. Soc.* **2000**, *122*, 1927–1936; (b) Holt, D. A.; Luengo, J. I.; Yamashita, D. S.; Oh, H.-J.; Konialian, A. L.; Yen, H.-K.; Rozamus, L. W.; Brandt, M.; Bossard, M. J.; Levy, M. A.; Eggleston, D. S.; Liang, J.; Schultz, L. W.; Stout, T. J.; Clardy, J. *J. Am. Chem. Soc.* **1993**, *115*, 9925–9938.
5. (a) Chang, Y.-H.; Pinnick, H. W. *J. Org. Chem.* **1978**, *43*, 373–374; (b) Tanikaga, R.; Yamada, S.; Nishikawa, T.; Matsui, A. *Tetrahedron* **1998**, *54*, 8933–8940.

6. Nájera, C.; Yus, M. *Tetrahedron* **1999**, *55*, 10547–10658.
7. Wratten, S. J.; Faulkner, D. J. *J. Org. Chem.* **1976**, *41*, 2465–2467.
8. (a) Trost, B. M.; Curran, D. P. *Tetrahedron Lett.* **1981**, *22*, 1287–1290; (b) Guerrero de la Rosa, V.; Ordóñez, M.; Llera, J. M. *Tetrahedron: Asymmetry* **2000**, *11*, 2991–3001.
9. (a) Siedlecka, R.; Skarżewski, J. *Synlett* **1996**, 757–758; (b) Lewanowicz, A.; Lipinski, J.; Siedlecka, R.; Skarżewski, J. *Tetrahedron* **1998**, *54*, 6571–6586.
10. Soai, K.; Kawase, Y.; Oshio, A. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1613–1615.
11. (a) Skarżewski, J.; Siedlecka, R.; Ostrycharz, E. *Tetrahedron: Asymmetry* **1999**, *10*, 3457–3461; (b) Skarżewski, J.; Ostrycharz, E.; Siedlecka, R.; Zielińska-Błajet, M.; Pisarski, B. *J. Chem. Res. (S)* **2001**, 263–264; *(M)* **2001**, 743–757.
12. (a) Bolm, C.; Bienewald, F. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2640–2642; (b) Bolm, C.; Bienewald, F. *Synlett* **1998**, 1327–1330.
13. (a) Mislow, K.; Green, M. M.; Laur, P.; Melillo, J. T.; Simmons, T.; Ternay, A. L. *J. Am. Chem. Soc.* **1965**, *87*, 1958–1976; (b) Jones, D. N.; Green, M. *J. Chem. Soc. (C)* **1967**, 532–542.
14. Rosini, C.; Donnoli, M. I.; Superchi, S. *Chem. Eur. J.* **2001**, *7*, 72–79.
15. (a) Ueno, Y.; Miyano, T.; Okawara, M. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 3615–3618; (b) Jensen, A. W.; Manczuk, J.; Nelson, D.; Caswell, O. *J. Heterocycl. Chem.* **2000**, *37*, 1527–1531.
16. (a) Redman, R. P.; Thomas, P. J.; Stirling, C. J. M. *J. Chem. Soc., Perkin Trans. 2* **1978**, 1135–1144; (b) Vorländer, D.; Friedberg, A. *Chem. Ber.* **1923**, *56*, 1148–1149.
17. Trost, B. M.; Arndt, H. C.; Strege, P. E.; Verhoeven, T. R. *Tetrahedron Lett.* **1976**, 3477–3478.
18. Dodson, R. M.; Hammen, P. D. *Chem. Commun.* **1968**, 1294–1296.