Lipase-Catalyzed Kinetic Resolution of γ-Hydroxy Phenyl Sulfones

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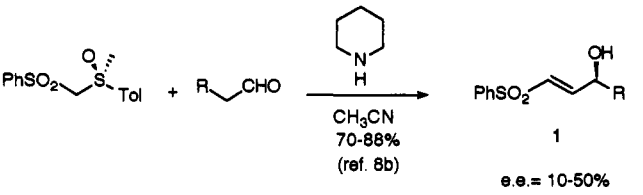
Lipase PS (from *Pseudomonas cepacia*) catalyzed the enantioselective transesterification of racemic γ-hydroxy-α,β-unsaturated phenyl sulfones **1** and their α,β-saturated derivatives **3** with vinyl acetate in an organic solvent (usually $^iPr_2O$). Remarkably, in substrates **1** with (*E*)-stereochemistry, the enantioselectivity of the process was little influenced by the nature of the R chain. Hence, very high enantiomeric ratios ($E \geq 45$) were observed in substrates **1** bearing short (R = Me or Et), long (R = n-C_6H_{13} or n-$C_{10}H_{21}$), bulky (R = ^{i}Pr), or functionalized R chains. The (*R*)-enantiomer was the fast-reacting enantiomer in all cases. Concerning the reactivity, the rate of the reaction decreased significantly with an increase in size or length of the R chain (reaction time for 50% conversion from 3.5 to 162 h). Less satisfactory enantioselectivities (E = 5–48) were obtained when the saturated substrates **3** were used instead of the corresponding α,β-unsaturated alcohols **1**.

Introduction

In recent years, considerable attention has been paid to synthetic applications of γ-hydroxy-α,β-unsaturated sulfones.[1] This versatile array of functionality has widely been used in highly stereocontrolled (C–C)-forming processes. Thus, the stereoselective conjugated addition of organometallics to cyclic and acyclic derivatives of γ-hydroxy-α,β-unsaturated sulfones has been studied by Fuchs'[2] and Isobe's[3] groups, respectively, and it has been applied to the synthesis of a wide variety of natural products.[4] Additionally, Trost and co-workers have recently reported[5] the inter- and intramolecular [3 + 2] cycloadditions of trimethylenemethane–palladium complexes to vinyl sulfones. Therefore, methods for the preparation of optically pure γ-hydroxy-α,β-unsaturated sulfones are of great importance in asymmetric synthesis. At present the Peterson olefination with enantiomerically pure α-alkoxy aldehydes[3,4,6] and the enantioselective reduction of β-sulfonyl enones[5a,7] are the main methods.

Recently we reported a practical one-step procedure for synthesis of racemic (*E*)-γ-hydroxy-α,β-unsaturated phenyl sulfones **1** by condensation of (arylsulfinyl)(phenylsulfonyl)methane with enolizable aldehydes.[8] This process involves a Knoevenagel condensation in tandem with an allylic sulfoxide–sulfenate rearrangement. However, when this reaction was carried out with enantiomerically pure (*S*)-(*p*-tolylsulfinyl)(phenylsulfonyl)methane (Scheme I), hydroxy sulfones **1** were obtained in moderate optical yields[8b] (10–50% ee).

Scheme I



At present there is a notable interest in the use of lipases as catalysts for the resolution of racemic alcohols.[9] Some of the reasons for the popularity of lipases are that they are readily available and relatively inexpensive, require no expensive cofactors, often exhibit high stereoselectivities with a wide range of substrates, and make the production of multigram quantities of optically enriched alcohols a facile laboratory procedure. Particularly, lipase-catalyzed acylation in nonaqueous media[10] has proved to be very advantageous over hydrolytic reactions. In this paper we describe the results obtained in the lipase-mediated acylation in organic media of structurally varied γ-hydroxy-α,β-unsaturated phenyl sulfones[11] and close derivatives[12] and the scope of the methodology.

Results

First, a kinetic study of the acylation of racemic (*E*)-4-(phenylsulfonyl)-3-buten-2-ol (**1a**, R = Me) was undertaken in several organic solvents, using eight commercially available lipases[13] and three acylating reagents ((2-chloroethyl)butyrate, butyric anhydride, and vinyl acetate).

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(13) Tested lipases were described as follows: *Porcine pancratin lipase* (PPL, Sigma), *Candida cilindracea lipase* (CCL, Sigma), *Mucor miehei lipase* (Amano), *Geotrictium candidum lipase* (lipase GC, Amano), *Rhizopus arrhizus lipase* (Fluka), *Penicillium roqueforti lipase* (lipase R, Amano), *C. cilindracea lipase* (lipase AY, Amano), and *Pseudomonas cepacia lipase* (lipase PS, Amano).

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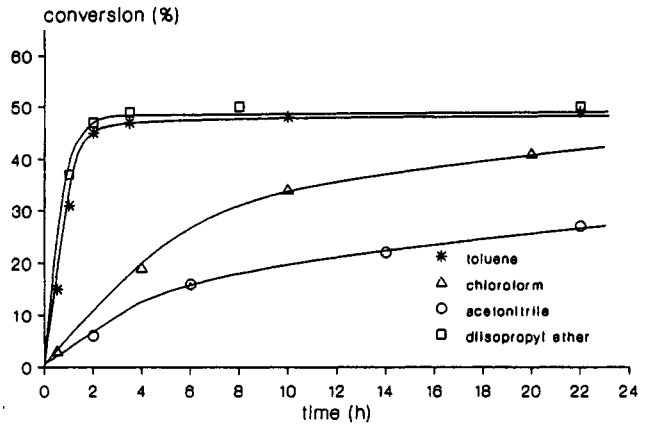
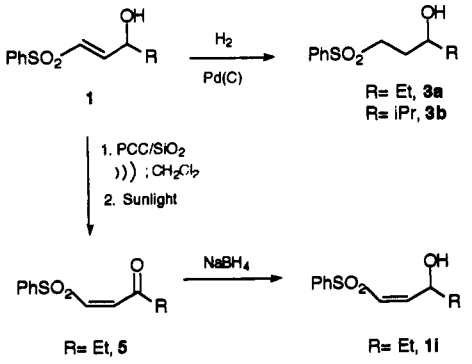


Figure 1. Conversion vs reaction time in the acetylation of **1a** with vinyl acetate (5 equiv), mediated by lipase PS (25 mg/mL), in different solvents. All reactions were run at room temperature and in the presence of molecular sieves (4 Å, 50 mg/mL).

Scheme II



The reactions were carried out at room temperature, in the presence of molecular sieves,[14] and the conversion was monitored by GC. Sluggish reactions were observed except for lipase PS (from *Pseudomonas cepacia*, Amano). Among the acylating reagents, vinyl acetate gave the best results. The effect of the solvent on the rate of this lipase-mediated acetylation is shown in Figure 1. Remarkably, in diisopropyl ether and toluene the reaction proceeded at a reasonable rate up to 50% conversion. In other solvents, such as chloroform and acetonitrile, the reaction becomes much slower.[15]

To isolate the products, in a further experiment the reaction in diisopropyl ether was stopped after 5.5 h (50% conversion) by filtration to remove the enzyme, and the resulting acetate **2a** and the unreacted alcohol were separated by flash chromatography in 47% and 46% yields, respectively. The optical purities of the unreacted alcohol (determined by ^{1}H-NMR analysis of its (*R*)-Mosher ester derivative[16]) and of the acetate **2a** (evaluated by ^{1}H-NMR using Pr(hfc)$_3$) were high (ee's >98% and >95%, respectively). **Therefore, the enantiomeric ratio (*E*)[17] of this kinetic resolution was excellent (*E* > 50).** The (*S*) configuration of unreacted alcohol **1a** was initially determined by analysis of the ^{1}H-NMR data for its Mosher ester derivative[16b] [(*R*)-MTPA]. In order to explore the scope of the kinetic resolution of γ-hydroxy phenyl sulfones mediated by lipase PS, the optimized enzymatic acylation conditions for **1a** were applied to a wide variety of substrates. The results are summarized in Tables I and II.

Scheme III

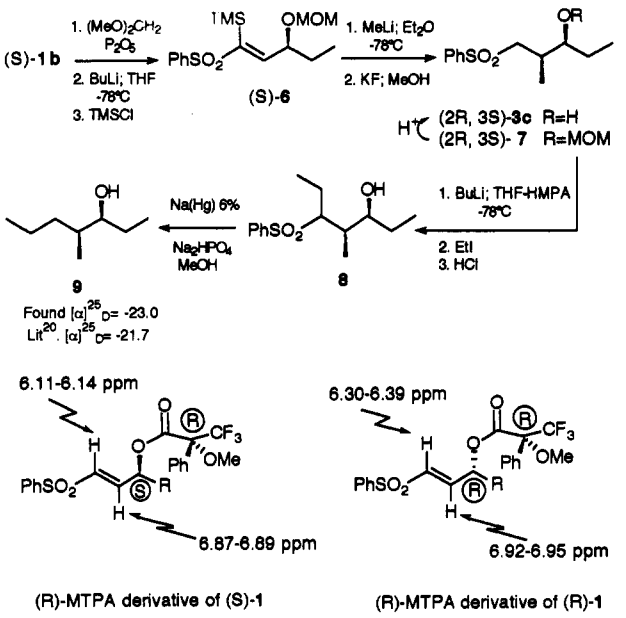


Figure 2. Configurational assignment of the enantiomeric alcohols **1** based on the ^{1}H-NMR chemical shifts of their (*R*)-MTPA derivatives. Values in $CDCl_3$.

All racemic α,β-unsaturated sulfones **1** of (*E*)-stereochemistry (**1a–1h**) were readily prepared in high yield by condensation of racemic (phenylsulfinyl)(phenylsulfonyl)methane with the corresponding aldehyde[8] (see also Scheme I). Racemic **1i** with a (*Z*)-stereochemistry was prepared in 65% overall yield from the (*E*)-stereoisomer (**1b**) by the three-step sequence shown in Scheme II. Oxidation of **1b** with PCC–silica gel under sonication[18] afforded the corresponding (*E*)-enone, which was quantitatively converted to the (*Z*)-stereoisomer **5** by photochemical isomerization under sunlight. Reduction of **5** with $NaBH_4$ gave racemic **1i** in 85% yield. The saturated γ-hydroxy sulfones **3** shown in Table II were readily prepared by catalytic hydrogenation (H_2, Pd(C)) of the unsaturated compounds **1b** and **1e**, respectively. Racemic alcohol **3c** was obtained by stereoselective conjugate addition of MeLi to the racemic α-trimethylsilyl derivative **6** following a previously reported procedure[19] (see also Scheme III).

In all cases the reactions were monitored by GC or ^{1}H-NMR; the acetate and unreacted alcohol products were easily separated by flash chromatography. The absolute (*S*)-stereochemistry of the remaining carbinols **1** was established by comparation of $[\alpha]_D$ data with the reported values of closely related γ-hydroxy-α,β-unsaturated sulfones[7,12a] (*p*-tolyl sulfones instead of phenyl sulfones) and by analysis of the ^{1}H-NMR data of their (*R*)-MTPA derivatives.[16b] The chemical shifts of both olefinic protons of the (*R*)-MTPA derivative of (*S*)-**1** appear significatively

(14) The presence of molecular sieves (4 Å) is essential in order to reach 50% conversion. For other examples of lipase-mediated acylations in the presence of molecular sieves see refs 22 and 23.

(15) For studies about the effect of the solvent in the reactivity and enantioselectivity of some lipase catalyzed reactions, see: (a) Sakurai, T.; Margolin, A. L.; Russell, A. J.; Klibanov, A. M. *J. Am. Chem. Soc.* **1988**, *110*, 7236. (b) Rubio, E.; Fernandez-Mayoralas, A.; Klibanov, A. M. *J. Am. Chem. Soc.* **1991**, *113*, 695. (c) Parida, S.; Dordick, J. S. *J. Am. Chem. Soc.* **1991**, *113*, 2253. (d) Nakamura, K.; Takebe, Y.; Kitayama, T.; Ohno, A. *Tetrahedron Lett.* **1991**, *32*, 4941.

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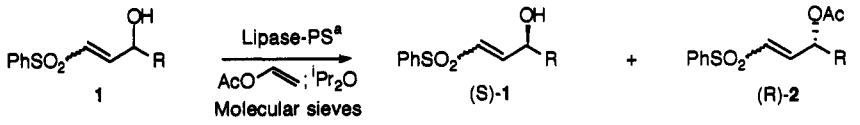
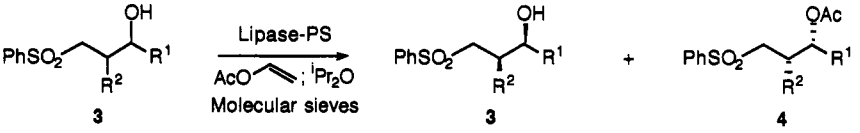
Table I. Enantioselective Acylation of γ-Hydroxy-α,β-unsaturated Phenyl Sulfones Mediated by Lipase PS



entry	substrate no.	R	conf[c]	time (h), convsn[d] (%)	recovered alcohol yield[b] (%); ee[e] (%) (conf); $[\alpha]_D$[f]	product acetate no.	product acetate yield[b] (%); ee[g] (%) (conf); $[\alpha]_D$[f]	E[h]
1	**1a**	Me	*E*	5.5, 50	46; >98 (*S*); +42.9	**2a**	47; >95 (*R*); +17.5	>50
2	**1b**	Et	*E*	3.5, 50	49; >98 (*S*); +45.3	**2b**	49; >95 (*R*); +16.7	>50
3	**1c**	n-C_6H_{13}	*E*	10, 50	48; >98 (*S*); +44.4	**2c**	47; >95 (*R*); +5.7	>50
4	**1d**	n-$C_{10}H_{21}$	*E*	47, 50	48; 88 (*S*); +32.4	**2d**	46; >95 (*R*); +3.9	45
5	**1e**	^{i}Pr	*E*	62, 50	46; 94 (*S*); +48.9	**2e**	48; >95 (*R*); +10.1	>50
6	**1f**	^{t}Bu	*E*	300, <5				
7	**1g**	$BnOCH_2CH_2$	*E*	16,[i] 50	48; 88 (*S*); -3.8	**2g**	47; >95 (*R*); +11.2	45
8	**1h**	$PhSO_2CH_2CH_2$	*E*	162,[j] 50	45; >98 (*S*); +11.9	**2h**	48; >95 (*R*); -2.8	>50
9	**1i**	Et	*Z*	100, <5				

[a] All reactions were performed at 50 mmol concentration of substrates 1, at rt, using 25 mg/mL of the enzyme, 5 equiv of vinyl acetate, and 50 mg/mL of powdered molecular sieves (4 Å). [b] In pure product after chromatography. [c] Configuration at the double bond. [d] Determined by capillary GC or ^{1}H-NMR integrals. [e] Determined via ^{1}H-NMR analysis of the Mosher ester derivative [(*R*)-MTPA]. [f] Values in $CHCl_3$ (*c* = 1). [g] Enantiomeric excess determined by ^{1}H-NMR using 0.1–0.3 equiv of Pr(hfc)$_3$. [h] Values determined from conversion and the ee of the recovered substrate as described.[17] No attempt was made to distinguish between values greater than 50 as *E* becomes increasingly sensitive to very small errors in measurement of ee's and conversion. [i] Reaction run in toluene due to the poor solubility of **1g** in ^{i}Pr$_2$O. [j] Reaction run in $CHCl_3$.

Table II. Enantioselective Acylation of γ-Hydroxy Phenyl Sulfones Mediated by Lipase PS



entry	substrate no.	R^1	R^2 (conf)	time (h), convsn[b] (%)	recovered alcohol yield[a] (%); ee[c] (%) (conf); $[\alpha]_D$[d]	product acetate no.	product acetate yield[a] (%); ee[e] (%) (conf); $[\alpha]_D$[d]	E[f]
1	**3a**	Et	H	3.5, 53	45; 92 (*S*); +23.0	**4a**	52; 80 (*R*); +12.3	48
2	**3b**	^{i}Pr	H	336, 50	48; 53 (*R*); +12.4	**4b**	47; 52 (*S*); +2.5	5
3	**3c**	Et	Me (syn)	96, 50	44; 91 (2*R*,3*S*); +1.3	**4c**	46; 84 (2*S*,3*R*); +29.8	30

[a] In pure product after chromatography. [b] Determined by ^{1}H-NMR integrals. [c] Determined via ^{1}H-NMR analysis of the (*R*)-MTPA ester derivative and by comparation with the $[\alpha]_D$ values of optically pure **3a** and **3b** obtained by hydrogenation of enantiomerically pure alcohols (*R*)-**1b** and (*R*)-**1e** (**3a** $[\alpha]_D$ +24.4; **3b** $[\alpha]_D$ +22.0). [d] Values in $CHCl_3$ (*c* = 1). [e] Determined by ^{1}H-NMR using 0.1–0.3 equiv of Pr(hfc)$_3$. [f] Values determined from conversion and the ee of the product acetate.[17]

shielded with respect to the diastereomer *R,R*. These values are shown in Figure 2. Additionally, the unreacted saturated alcohols **3a–c** were correlated with the unsaturated alcohols (*S*)-**1b** and (*S*)-**1e** according to the reactions shown in Schemes II and III.

This configurational assignment was confirmed in the case of the lipase-acetylation of racemic **1b** by chemical correlation of the unreacted alcohol (*S*)-**1b** with the elm bark beetle aggregation pheromone (−)-(3*S*,4*S*)-4-methyl-3-heptanol[20] (**9**) (Scheme III). The alcohol (*S*)-**1b** was initially converted into the corresponding MOM derivative, which was metalated at the α-position with nBuLi in THF at −78 °C and then silylated (CITMS) to afford (*S*)-**6** in 80% overall yield.[19] Compound (*S*)-**6** was readily transformed into sulfone (2*R*,3*S*)-**7** (92% yield) via highly syn-stereoselective conjugate addition of MeLi at −78 °C in Et_2O (syn:anti > 98:2)[19] followed by desilylation with KF. Deprotonation of **7** with nBuLi, followed by alkylation with EtI and acidic hydrolysis of the acetal moiety, gave sulfones **8** (88% yield) as a 5:1 mixture of stereoisomers. Finally, sulfones **8** were transformed into the enantiomerically pure pheromone **9** by reductive cleavage of the phenylsulfonyl group[21] [found $[\alpha]^{25}_D$ = −23.0 (*c* = 1, hexane) (lit.[20] $[\alpha]^{25}_D$ = −21.7 (hexane))].

Discussion

From the results of Table I it should be pointed out that the enantioselectivity of the enzymatic acetylation of allylic alcohols **1** is almost independent of the increasing length or size of the R group. Except for compounds **1f** (entry 6) and **1i** (entry 9), the lipase PS mediated acetylation of substrates **1** is very efficient. The reactions occur with very high values of the selectivity factors (usually $E > 50$) and the same sense of enantioselection. In all cases we observed that the acetylation was extremely slow with conversions approaching 50%, and the (*R*) enantiomer was the most reactive. Acylations of alcohols **1a–d** (entries 1–4), which bear progressively longer unbranched aliphatic chains (R from C_1 to C_{10} chain length), were all very enantioselective ($E \geq 45$). However, the initial rate of acylation decreases with the increasing length of R chain; for instance, acetylation of **1b** is about 10 times faster than that of **1d**. Moreover, alcohols **1g** (entry 7) and **1h** (entry 8) with functionalized R chains have also been efficiently resolved ($E = 45$ and >50, respectively). These results are particularly important because the functionalized R chain

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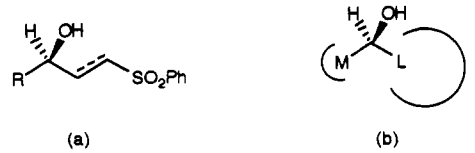

Figure 3. (a) Fast-reacting enantiomer in the acetylation mediated by lipase PS. (b) Fast-reacting enantiomer according to a reported rule.[24]

in the resolved alcohols (*S*)-**1g** and (*S*)-**1h** or in the corresponding acetates (*R*)-**2g** and (*R*)-**2h** could be easily manipulated to elaborate complex side chains for a wide range of synthetic applications.

The results obtained with alcohols **1b** (*R* = Et), **1e** (R = ^{i}Pr), and **1f** (R = ^{t}Bu) show the effect of the increasing size of the R group in the reactivity and enantioselectivity of this enzymatic reaction. Thus, despite the large steric requirement of the ^{i}Pr group, alcohol **1e** (entry 5) was enantioselectively acetylated[22] (*E* > 50), although the rate was about 20 times slower than that of **1b** (entry 2). By contrast, no acetylation was observed for alcohol **1f** (entry 6) after 10 days of reaction, showing that alcohols **1** with very big R groups are not substrates for the enzyme.

On the other hand, entry 9 clearly shows that the required stereochemistry at the double bond in substrates **1** must be (*E*) in order to be acetylated by lipase PS/vinyl acetate; less than 5% conversion was observed in the acetylation of **1i** ((*Z*) stereochemistry) after 100 h. Similar results have previously been reported by Burgess[23] in the acetylation of (*E*)- and (*Z*)-4-phenylbut-3-en-2-ol mediated by lipase AK (from *Pseudomonas* sp.).

The comparison of data of Table II with the corresponding data of Table I shows that the enantioselectivity of the enzymatic reaction was lower for saturated sulfones **3** than α,β-unsaturated sulfones **1**; however, the sense of enantiodiscrimination was the same. Thus, alcohol **3a** (R = Et, entry 1) was acetylated at a rate similar to that of **1b** (entry 2, Table I), but with a slightly lower enantioselectivity (*E* = 48 instead of *E* > 50). Larger differences were obtained for **3b** (entry 2) and **1e** (entry 6, Table I). Substrate **3b** (R = ^{i}Pr) was acetylated with lipase PS/vinyl acetate more slowly than **1e** (R = ^{i}Pr) and with low enantioselectivity. These results indicate that enantiomerically pure γ-hydroxy phenyl sulfones **3** are best prepared by initially resolving the corresponding (*E*)-γ-hydroxy-α,β-unsaturated phenyl sulfones **1** followed by hydrogenation (H_2/Pd/C) of the double bond. The data obtained in the enzymatic resolution of alcohol **3c** (entry 3), which has a methyl substituent at the β-position, are also interesting. This substrate was acetylated very much slowly than **3a**, as would be expected from the increase in steric bulk near the hydroxymethine group, and with a slightly lower enantioselectivity.

It should be noted that the sense of enantioselection of lipase PS (from *Pseudomonas cepacia*) is the same for all the examples shown in Tables I and II, in spite of different lengths and steric sizes of the R substituents. This behavior seems to be more general than the reported for the enzymatic resolution of γ-hydroxy-α,β-unsaturated methyl esters by lipase from *Pseudomonas* sp. (Amano AK).[22,23] In all cases the enantiomer indicated in Figure 3a is acylated preferentially; this enantiomer has (*R*)-configuration except for **1f** and **3b** where the priority of the substituents bonded to the hydroxymethyne moiety was reversed. Our results do not obey the recent reported rule[24] for predicting the fast-reacting enantiomer in the resolution of secondary alcohols mediated by lipase PS (Figure 3b), unless the chain containing the phenylsulfonyl group is arbitrarily assigned as the "large group" regardless of the steric size of R. This fact suggests that bulky functionalities (such as the phenylsulfonyl group) slightly removed from the chiral center should be taken into account in order to elaborate more refined models. A similar assumption has been recently proposed for the resolutions of secondary alcohols mediated by crude lipase from *Pseudomonas* sp.[23]

(22) This result is in contrast with that recently reported by Burgess et al. in the enzymatic resolution of γ-hydroxy-α,β-unsaturated methyl esters mediated by lipase from *Pseudomonas* sp. (Amano AK). These authors noticed that when R was ^{i}Pr the enantioselectivity of the process was poor (*E* = 1.6) and reversed ((*S*) enantiomer the most reactive). Burgess, K.; Henderson, J. *Tetrahedron Asymmetry* **1990**, *1*, 57.

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Conclusions

A wide variety of γ-hydroxy-α,β-unsaturated phenyl sulfones of (*E*) configuration have been efficiently resolved by enantioselective acetylation mediated by lipase PS in organic solvent by using vinyl acetate as the acylating agent. A uniform sense of enantioselection and high enantioselectivities (*E* ≥ 45) were observed in substrates bearing short (R = Me, Et), long (R = n-$C_{10}H_{21}$), bulky (R = ^{i}Pr), or functionalized R chains bonded to the hydroxymethine group. It was observed that increasing the size or length of the R group results in lower reactivity. Substrates **1** of (*Z*)-configuration or with very bulky R chains (R = ^{t}Bu) did not react under these conditions. Lower enantioselectivities were observed when γ-hydroxy-α,β-saturated phenyl sulfones **3** were used as substrates.

The ready access to racemic (*E*)-γ-hydroxy-α,β-unsaturated phenyl sulfones[8] (**1**), coupled with their efficient and simple enzymatic resolution, make vinyl sulfones **1** very attractive as chiral building blocks for asymmetric synthesis.

Experimental Section

Melting points are uncorrected. ^{1}H-NMR and ^{13}C-NMR spectra were recorded in $CDCl_3$. Chemical shifts are reported in parts per million (ppm) relative to Me_4Si. Mass spectra (MS) were determined at an ionizing voltage of 70 eV. Mass data are reported in mass units (*m*/*z*), and the values in brackets regard the relative intensity from base peak (as 100%). Lipase PS (from *P. cepacia*) was purchased from Amano Pharm. Co. All solvents were dried before use. THF was distilled from sodium–benzophenone under argon. Acetonitrile and $CHCl_3$ were distilled from P_2O_5. Propionaldehyde was distilled prior to use. Butyraldehyde, octyl aldehyde, dodecyl aldehyde, isovaleraldehyde, and 3,3-dimethylbutyraldehyde were purchased from Aldrich and used without further purification. Flash column chromatographies were performed with silica gel Merck-60 (230–400 mesh).

General Procedure for the Preparation of (±)-(*E*)-γ-Hydroxy-α,β-unsaturated Phenyl Sulfones (1a–h). To a solution of 0.68 mmol (200 mg, 1.0 equiv) of (phenylsulfonyl)(*p*-tolylsulfinyl)methane[8b] in 3 mL of dry acetonitrile, cooled at 0 °C, were added sequentially 1.36 mmol (134 μL, 2.0 equiv) of piperidine and 1.36 mmol (2.0 equiv) of the corresponding aldehyde. Stirring was continued for 1–8 h at 0 °C. Then, 5% HCl (10 mL) was added and the reaction mixture was extracted with CH_2Cl_2 (2 × 15 mL). The combined organic layers were dried (Na_2SO_4) and evaporated. The crude product was purified by flash chromatography to afford pure unsaturated sulfones **1a–h** (the eluent is indicated for each compound). The compounds **1a**, **1c**, **1e**, and **1g** have been previously reported.[8b]

(±)-(*E*)-1-(Phenylsulfonyl)-1-penten-3-ol (1b). Starting aldehyde: butyraldehyde. Reaction time: 3.5 h. Yield: 92% (dichloromethane–acetone (80:1)). Mp: 44–6 °C.

(±)-(*E*)-1-(Phenylsulfonyl)-1-tridecen-3-ol (1d). Starting aldehyde: dodecyl aldehyde. Reaction time: 4 h. Yield: 85%

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(hexane–ethyl acetate (3:1)). Mp: 68–9 °C.

(±)-(*E*)-4,4-Dimethyl-1-(phenylsulfonyl)-1-penten-3-ol (1f). Starting aldehyde: 3,3-dimethylbutyraldehyde. Reaction time: 8 h. Yield 72% (hexane–ethyl acetate (3:1)). Mp: 83–5 °C. ^{1}H-NMR δ: 7.90 (m, 2 H, $PhSO_2$), 7.60 (m, 3 H, $PhSO_2$), 7.10 (dd, 1 H, J = 15.0 and 4.0 Hz, C*H*=CHS), 6.62 (dd, 1 H, J = 15.0 and 1.8 Hz, CH=C*H*S), 4.04 (dd, 1 H, J = 4.0 and 1.8 Hz, C*H*OH), 1.85 (br s, 1 H, OH), and 0.94 (s, 9 H, ^{t}Bu). ^{13}C-NMR δ: 146.6, 140.0, 133.2, 130.5, 129.1, 127.2, 77.4, 35.7, and 25.5. Anal. Calcd for $C_{13}H_{18}O_3S$: C, 61.47; H, 7.14; S, 12.62. Found: C, 61.70; H, 7.03; S, 12.58.

(±)-(*E*)-1,5-Bis(phenylsulfonyl)-1-penten-3-ol (1h). Starting aldehyde: 4-(phenylsulfonyl)butyraldehyde. Reaction time: 7 h. Yield: 83% (hexane–ethyl acetate (2:1)). Mp: 109–110 °C.

(±)-(*Z*)-1-(Phenylsulfonyl)-1-penten-3-ol (1i). Commercial-grade PCC (6.64 mmol) was ground with silica gel (1 wt equiv) in a mortar. The resulting free-running light orange solid was suspended in CH_2Cl_2 (20 mL) and was inserted in a ultrasonic processor beneath the surface (1 cm) of the suspension at 18 °C (water bath). The alcohol **1b** (1.0 g, 4.42 mmol) in CH_2Cl_2 (5 mL) was added in one portion. The reaction was stopped after 2 h, the brown suspension was diluted with ether (20 mL) and vacuum filtered through a Buchner funnel packed with Celite, and the granular brown residue was washed with ether (150 mL). The resulting filtrate was concentrated and purified by flash chromatography (hexane–ethyl acetate (2:1)) to afford 800 mg of the (*E*)-enone **5** (80% yield). ^{1}H-NMR δ: 7.92 (m, 2 H, $PhSO_2$), 7.61 (m, 3 H, $PhSO_2$), 7.18 and 7.06 (AB sistem, 2 H, J = 15.2 Hz, CH=CH), 2.67 (q, 2 H, J = 7.2 Hz, CH_2), and 1.12 (t, 3 H, J = 7.2 Hz, CH_3). ^{13}C-NMR δ: 198.2, 140.1, 138.5, 135.4, 134.3, 129.6, 128.2, 35.9, and 7.3. Anal. Calcd for $C_{11}H_{12}O_3S$: C, 58.93; H, 5.39; S, 14.30. Found: C, 59.05; H, 5.44; S, 114.28. The (*E*)-enone **5** was quantitatively isomerized to the (*Z*)-stereoisomer by exposing a solution of 700 mg of (*E*)-enone **5** in $CHCl_3$ (100 mL) to sunlight for 4 days. ^{1}H-NMR δ: 7.96 (m, 2 H, $PhSO_2$), 7.63 (m, 3 H, $PhSO_2$), 6.64 and 6.39 (AB sistem, 2 H, J = 11.6 Hz, CH=CH), 2.81 (q, 2 H, J = 7.2 Hz, CH_2) and 1.21 (t, 3 H, J = 7.2 Hz, CH_3). ^{13}C-NMR δ: 203.5, 141.6, 139.2, 134.1, 132.4, 129.4, 128.2, 36.9, and 7.2. To a solution of (*Z*)-enone **5** (500 mg) in MeOH (25 mL) was slowly added at rt a solution of sodium borohydride (168 mg, 4.46 mmol) in MeOH (25 mL). After 4 h at rt a solution of aqueous NH_4Cl (50 mL) was added. The mixture was extracted with ether (2 × 50 mL), and the combined organic layers were washed with water (2 × 50 mL), dried (Na_2SO_4), and evaporated. The residue was purified by chromatography (hexane–ethyl acetate (2:1)) to afford 429 mg of **1i** (85% yield). IR ($CHCl_3$): 3340, 2920, 1560, 1420, 1280, and 1125 cm^{-1}. ^{1}H-NMR δ: 7.91 (m, 2 H, $PhSO_2$), 7.60 (m, 3 H, $PhSO_2$), 6.29 (d, 1 H, J = 2 Hz, OH), 6.30 and 6.22 (AB system, 2 H, J = 11.3 Hz, CH=CH), 5.15 (m, 1 H, C*H*OH), 1.62 (m, 2 H, CH_2), and 0.97 (t, 3 H, J = 7.4 Hz, CH_3).

(±)-1-(Phenylsulfonyl)-3-pentanol (3a). A solution of 400 mg of **1b** in 50 mL of EtOH was hydrogenated with 40 mg of 10% Pd/C catalyst under 3 psi of hydrogen for 24 h. The catalyst was removed by filtration, and the filtrate was evaporated to afford 387 mg of **3a** (96% yield).

(±)-4-Methyl-1-(phenylsulfonyl)-3-pentanol (3b). Prepared by the above method starting from **1e**. Yield: 94%.

(±)-*threo*-2-Methyl-1-(phenylsulfonyl)-3-pentanol (3c). To a solution of 900 mg of racemic **7** in THF (50 mL) was added 6 M HCl (30 mL). The mixture was stirred at room temperature for 5 h. Then, a saturated solution of aqueous $NaHCO_3$ (20 mL) was added, the organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were dried (Na_2SO_4) and evaporated. The residue was purified by flash chromatography (hexane–ethyl acetate (2:1)) to afford 723 mg of **3c** (95% yield).

General Procedure for the Lipase-Mediated Acylation of Compounds 1 and 3. Five equiv of vinyl acetate, 25 mg/mL of lipase PS, and 50 mg/mL of powdered molecular sieves (4 Å) were added sequentially to a solution (50 mM) of racemic alcohols **1** (or **3**). The resulting suspension was vigorously shaken at rt and monitored by GC or ^{1}H-NMR for the conversion. When 50% conversion was reached, the enzyme and the molecular sieves were filtered off and the solvent was evaporated. The residue was purified by flash chromatography to afford the unreacted alcohols (**1** or **3**) and the corresponding acetates **2** (or **4**) (the eluent is indicated below for each case). The ee's of unreacted alcohols were determined via ^{1}H-NMR analysis of their (*R*)-MTPA ester derivatives,[16] whereas the ee's of the acetates were evaluated by ^{1}H-NMR using Pr(hfc)$_3$ as chiral shift reagent.

(*S*)-(*E*)-4-(Phenylsulfonyl)-3-buten-2-ol [(*S*)-1a]. A solution of 530 mg of (±)-**1a** (2.5 mmol) in 50 mL of ^{i}Pr$_2$O was acetylated for 5.5 h. A total of 298 mg of (*R*)-**2a** (47%) and 242 mg of (*S*)-**1a** (46%) was obtained (hexane–ethyl acetate (3:1)). Mp: 94–5 °C. Ee: >98%. $[\alpha]^{25}_D$: +42.9 (c = 1, $CHCl_3$). For IR, ^{1}H-NMR, ^{13}C-NMR, and MS see ref 8b. Anal. Calcd for $C_{10}H_{12}O_3S$: C, 56.58; H, 5.70; S, 15.11. Found: C, 56.85; H, 6.00; S, 14.86.

Acetate (*R*)-2a. Ee: >95%. $[\alpha]^{25}_D$: +17.5 (c = 1, $CHCl_3$). IR (neat): 3060, 2990, 2940, 1735, 1235, and 1150 cm^{-1}. ^{1}H-NMR δ: 7.90 (m, 2 H, $PhSO_2$), 7.60 (m, 3 H, $PhSO_2$), 6.93 (dd, 1 H, J = 15.2 and 4.2 Hz, C*H*=CHS), 6.48 (dd, 1 H, J = 15.0 and 1.7 Hz, CH=C*H*S), 5.52 (m, 1 H, C*H*OAc), 2.07 (s, 3 H, CH_3CO_2) and 1.38 (d, 3 H, J = 6.7 Hz, CH_3CH). ^{13}C-NMR δ: 169.5, 144.2, 139.7, 133.5, 130.1, 129.3, 127.6, 67.8, 20.8, and 19.3. MS: 212 (6, M$^+$ − 44), 169 (21), 125 (51), 113 (59), 77 (73), 71 (100). Anal. Calcd for $C_{12}H_{14}O_4S$: C, 56.68; H, 5.55; S, 12.61. Found: C, 56.97; H, 5.37; S, 12.51.

(*S*)-(*E*)-1-(Phenylsulfonyl)-1-penten-3-ol [(*S*)-1b]. A solution of 2.26 g of (±)-**1b** (10 mmol) in 200 mL of ^{i}Pr$_2$O was acetylated for 3.5 h. A total of 1.34 g of (*R*)-**2b** (49%) and 1.13 g of (*S*)-**1b** (49%) was obtained (hexane–ethyl acetate (3:1)). Mp: 60–2 °C. Ee: >98%. $[\alpha]^{25}_D$: +45.3 (c = 1, $CHCl_3$). IR (neat): 3500, 3065, 2985, 1630, 1450, 1265, 1140, and 1090 cm^{-1}. ^{1}H-NMR δ: 7.90 (m, 2 H, $PhSO_2$), 7.60 (m, 3 H, $PhSO_2$), 7.00 (dd, 1 H, J = 15.1 and 3.8 Hz, C*H*=CHS), 6.61 (dd, 1 H, J = 14.9 and 1.6 Hz, CH=C*H*S), 4.35 (m, 1 H, C*H*OH), 1.66 (m, 3 H, OH and CH2), and 0.97 (t, 3 H, J = 7.4 Hz, CH_3). ^{13}C-NMR δ: 148.3, 140.0, 133.3, 129.3, 129.2, 127.4, 71.1, 29.1, and 9.3. MS: 197 (18, M$^+$ − 29), 169 (100), 125 (88), 91 (11), 77 (27). Anal. Calcd for $C_{11}H_{14}O_3S$: C, 58.38; H, 6.24; S, 14.17. Found: C, 58.39; H, 5.98; S, 14.02.

Acetate (*R*)-2b. Ee: >95%, $[\alpha]^{25}_D$: +16.7 (c = 1, $CHCl_3$). ^{1}H-NMR δ: 7.90 (m, 2 H, $PhSO_2$), 7.60 (m, 3 H, $PhSO_2$), 6.92 (dd, 1 H, J = 15.1 and 4.5 Hz, C*H*=CHS), 6.46 (dd, 1 H, J = 15.1 and 1.7 Hz, CH=C*H*S), 5.42 (m, 1 H, C*H*OAc), 2.08 (s, 3 H, CH_3CO_2), 1.72 (m, 2 H, CH_2), and 0.91 (t, 3 H, J = 7.4 Hz, CH_3CH_2). ^{13}C-NMR δ: 169.6, 143.3, 139.7, 133.4, 130.7, 129.2, 127.5, 72.2, 26.5, 20.7, and 8.9. MS: 268 (7, M$^+$), 226 (16, M$^+$ − 42), 197 (51), 169 (51), 143 (17), 127 (100), 125 (74), 85 (87), 77 (63). Anal. Calcd for $C_{13}H_{16}O_4S$: C, 58.19; H, 6.01; S, 11.95. Found: C, 58.20; H, 5.97; S, 11.82.

(*S*)-(*E*)-1-(Phenylsulfonyl)-1-nonen-3-ol [(*S*)-1c]. A solution of 127 mg of (±)-**1c** (0.45 mmol) in 9 mL of ^{i}Pr$_2$O was acetylated for 10 h. A total of 69 mg of (*R*)-**2c** (47%) and 61 mg of (*S*)-**1c** (48%) was obtained (hexane–ethyl acetate (5:1)). Mp: 64–5 °C. Ee: >98%. $[\alpha]^{25}_D$: +44.4 (c = 1, $CHCl_3$). For IR, ^{1}H-NMR, ^{13}C-NMR, and MS see ref 8b. Anal. Calcd for $C_{15}H_{22}O_3S$: C, 63.79; H, 7.86; S, 11.36. Found: C, 63.66; H, 7.66; S, 11.21.

Acetate (*R*)-2c. Ee: >95%. $[\alpha]^{25}_D$: +5.7 (c = 1, $CHCl_3$). ^{1}H-NMR δ: 7.90 (m, 2 H, $PhSO_2$), 7.60 (m, 3 H, $PhSO_2$), 6.92 (dd, 1 H, J = 15.0 and 4.6 Hz, C*H*=CHS), 6.45 (dd, 1 H, J = 15.2 and 1.6 Hz, CH=C*H*S), 5.46 (m, 1 H, C*H*OAc), 2.07 (s, 3 H, CH_3CO_2), 1.67 (m, 2 H, CH_2CHOAc), 1.26 (m, 8 H, $(CH_2)_4$), and 0.87 (t, 3 H, J = 6.7 Hz, CH_3CH_2). ^{13}C-NMR δ: 169.6, 143.6, 139.9, 133.4, 130.5, 129.2, 127.5, 71.3, 33.4, 31.3, 28.7, 24.6, 22.3, 20.7, and 13.9. MS: 282 (3, M$^+$ − 42), 183 (73), 141 (100), 125 (46), 113 (18), 77 (26). Anal. Calcd for $C_{17}H_{24}O_4S$: C, 62.93; H, 7.46; S, 9.88. Found: C, 62.71; H, 7.35; S, 9.70.

(*S*)-(*E*)-1-(Phenylsulfonyl)-1-tridecen-3-ol [(*S*)-1d]. A solution of 338 mg of (±)-**1d** (1 mmol) in 20 mL of ^{i}Pr$_2$O was acetylated for 47 h. A total of 173 mg of (*R*)-**2d** (46%) and 164 mg of alcohol (*S*)-**1d** (48%) was obtained (hexane–ethyl acetate (3:1)). Mp: 65–7 °C. Ee: 88%. $[\alpha]^{25}_D$: +32.4 (c = 1, $CHCl_3$). IR ($CHCl_3$): 3400, 2900, 2830, 1305, 1295, 1130, and 1075 cm^{-1}. ^{1}H-NMR δ: 7.90 (m, 2 H, $PhSO_2$), 7.60 (m, 3 H, $PhSO_2$), 7.00 (dd, 1 H, J = 14.9 and 3.7 Hz, C*H*=CHS), 6.60 (dd, 1 H, J = 14.9 and 1.9 Hz, CH=C*H*S), 4.38 (m, 1 H, C*H*OH), 1.80 (br s, 1 H, OH), 1.58 (m, 2 H, CH_2CH), 1.25 (br s, 16 H, $(CH_2)_8$), and 0.88 (t, 3 H, J = 6.8 Hz, CH_3). ^{13}C-NMR δ: 148.8, 140.1, 133.2, 129.1, 127.3,

69.9, 36.0, 31.7, 29.4, 29.2, 25.0, 22.5, and 13.9. MS: 197 (18, M^+ - 29), 169 (100), 125 (88), 91 (11), 77 (27). Anal. Calcd for $C_{19}H_{30}O_3S$: C, 67.51; H, 8.95; S, 9.49. Found: C, 67.80; H, 8.82; S, 9.58.

Acetate (*R*)-2d. Ee: >95%. $[\alpha]^{25}_D$: +3.9 (c = 1, $CHCl_3$). IR ($CHCl_3$): 2900, 2830, 1305, 1725, 1305, 1215, 1130, and 1075 cm^{-1}. ^{1}H-NMR δ: 7.90 (m, 2 H, $PhSO_2$), 7.60 (m, 3 H, $PhSO_2$), 6.92 (dd, 1 H, J = 15.1 and 4.7 Hz, C*H*=CHS), 6.44 (dd, 1 H, J = 15.1 and 1.6 Hz, CH=C*H*S), 5.45 (ddt, 1 H, J = 6.3, 4.6 and 1.7 Hz, C*H*OAc), 2.07 (s, 3 H, CH_3CO_2), 1.65 (m, 2 H, CH_2CHOAc), 1.25 (m, 16 H, $(CH_2)_8$), and 0.88 (t, 3 H, J = 6.7 Hz, CH_3). ^{13}C-NMR δ: 169.5, 143.6, 139.9, 133.3, 130.5, 129.1, 127.5, 71.2, 33.4, 31.7, 29.3, 29.1, 29.0, 24.6, 22.5, 20.7, and 13.9. Anal. Calcd for $C_{21}H_{32}O_4S$: C, 66.37; H, 8.49; S, 8.44. Found: C, 66.22; H, 8.70; S, 8.61.

(*S*)-(*E*)-4-Methyl-1-(phenylsulfonyl)-1-penten-3-ol [(*S*)-1e]. A solution of 120 mg of (±)-**1e** (0.5 mmol) in 10 mL of $^iPr_2O$ was acetylated for 62 h. A total of 68 mg of (*R*)-**2e** (48%) and 55 mg of (*S*)-**1e** (46%) was obtained (hexane–ethyl acetate (3:1)). Mp: 61–3 °C. Ee: 94%. $[\alpha]^{25}_D$: +48.9 (c = 1, $CHCl_3$). For IR, ^{1}H-NMR, ^{13}C-NMR, and MS see ref 8b. Anal. Calcd for $C_{12}H_{16}O_3S$: C, 59.97; H, 6.71; S, 13.34. Found: C, 60.15; H, 6.47; S, 13.20.

Acetate (*R*)-2e. Ee: >95%. Mp: 67–8 °C. $[\alpha]^{25}_D$: +10.1 (c = 1, $CHCl_3$). IR ($CHCl_3$): 1725, 1310, 1220, 1135, and 1075 cm^{-1}. ^{1}H-NMR δ: 7.90 (m, 2 H, $PhSO_2$), 7.60 (m, 3 H, $PhSO_2$), 6.93 (dd, 1 H, J = 15.1 and 4.7 Hz, C*H*=CHS), 6.44 (dd, 1 H, J = 15.2 and 1.6 Hz, CH=C*H*S), 5.33 (ddd, 1 H, J = 6.7, 4.1, and 1.7 Hz, C*H*OAc), 2.08 (s, 3 H, CH_3CO_2), 2.01 (m, 1 H, CH_3), 0.94 (d, 3 H, J = 6.8 Hz, CH_3), and 0.91 (d, 3 H, J = 6.8 Hz, $(CH_3)_2$CH). ^{13}C-NMR δ: 169.7, 142.4, 139.9, 133.5, 131.4, 129.3, 127.5, 75.5, 31.9, 20.7, 17.8, and 17.5. Anal. Calcd for $C_{14}H_{18}O_4S$: C, 59.55; H, 6.42; S, 11.36. Found: C, 59.79; H, 6.52; S, 11.35.

(*S*)-(*E*)-5-(Benzyloxy)-1-(phenylsulfonyl)-1-penten-3-ol [(*S*)-1g]. A solution of 133 mg of (±)-**1g** (0.4 mmol) in 8 mL of toluene was acetylated for 16 h. A total of 70 mg of (*R*)-**2g** (47%) and 64 mg of (*S*)-**1g** (48%) was obtained (hexane–ethyl acetate (2:1)). Mp: 64–6 °C. Ee: 88%. $[\alpha]^{25}_D$: −3.8 (c = 1, $CHCl_3$). For IR, ^{1}H-NMR, and ^{13}C-NMR see ref 8b. Anal. Calcd for $C_{18}H_{20}O_4S$: C, 65.04; H, 6.06; S, 9.65. Found: C, 65.16; H, 6.13; S, 9.42.

Acetate (*R*)-2g. Ee: >95%. $[\alpha]^{25}_D$; +11.2 (c = 1, $CHCl_3$). ^{1}H-NMR δ: 7.87 (m, 2 H, $PhSO_2$), 7.55 (m, 3 H, $PhSO_2$), 7.30 (m, 5 H, Ph), 6.95 (dd, 1 H, J = 15.0 and 4.7 Hz, C*H*=CHS), 6.44 (dd, 1 H, J = 15.0 and 1.6 Hz, CH=C*H*S), 5.64 (m, 1 H, C*H*OAc), 4.45 (s, 2 H, OCH_2Ph), 3.49 (t, 2 H, J = 5.9 Hz, CH_2O) 2.02 (s, 3 H, CH_3CO_2), and 1.97 (m, 2 H, CH_2CH). ^{13}C-NMR δ: 169.5, 143.5, 139.8, 137.8, 133.4, 130.6, 129.2, 128.3, 127.6, 73.0, 69.1, 65.2, 33.8, and 20.7. MS: 314 (4), 208 (14), 173 (23), 163 (20), 143 (9), 125 (23), 91 (100), 77 (13). Anal. Calcd for $C_{20}H_{22}O_5S$: C, 64.15; H, 5.92; S, 8.56. Found: C, 63.72; H, 6.03; S, 8.43.

(*S*)-(*E*)-1,5-Bis(phenylsulfonyl)-1-penten-3-ol [(*S*)-1h]. A solution of 366 mg of (±)-**1h** (1 mmol) in 20 mL of $CHCl_3$ was acetylated for 162 h. A total of 196 mg of (*R*)-**2h** (48%) and 165 mg of (*S*)-**1h** (45%) was obtained (hexane–ethyl acetate (1:2)). Mp: 99–101 °C. Ee: >98%. $[\alpha]^{25}_D$: +11.9 (c = 1, $CHCl_3$). IR ($CHCl_3$): 3450, 1570, 1435, 1300, 1135, and 1075 cm^{-1}. ^{1}H-NMR δ: 7.87 (m, 4 H, $PhSO_2$ × 2), 7.58 (m, 6 H, $PhSO_2$ × 2), 6.90 (dd, 1 H, J = 14.9 and 3.6 Hz, C*H*=CHS), 6.64 (dd, 1 H, J = 15.0 and 1.8 Hz, CH=C*H*S), 4.60 (m, 1 H, C*H*OH), 3.21 (m, 2 H, CH_2SO_2), 2.85 (br s, 1 H, OH), 2.11 (m, 1 H), and 1.93 (m, 1 H). ^{13}C-NMR δ: 146.3, 139.8, 138.6, 134.0, 133.6, 130.9, 129.4, 127.9, 127.6, 67.8, 52.1, and 28.7. Anal. Calcd for $C_{17}H_{18}O_5S_2$: C, 55.72; H, 4.95; S, 17.50. Found: C, 55.53; H, 4.92; S, 17.35.

Acetate (*R*)-2h. Mp: 84–6 °C. Ee >95%. $[\alpha]^{25}_D$: −2.8 (c = 1, $CHCl_3$). IR ($CHCl_3$): 1730, 1435, 1310, 1215, 1135, and 1075 cm^{-1}. ^{1}H-NMR δ: 7.85 (m, 4 H, $PhSO_2$ × 2), 7.53 (m, 6 H, $PhSO_2$ × 2), 6.79 (dd, 1 H, J = 15.1 and 4.4 Hz, C*H*=CHS), 6.46 (dd, 1 H, J = 15.1 and 1.6 Hz, CH=C*H*S), 5.53 (ddt, 1 H, J = 6.8, 4.8, and 1.6 Hz, C*H*OAc), 3.07 (m, 2 H, CH_2SO_2), 2.11 (m, 2 H, CH_2), and 2.02 (s, 3 H, CH_3CO_2). ^{13}C-NMR δ: 169.3, 141.2, 139.4, 138.4, 134.0, 133.7, 132.3, 129.4, 127.9, 127.6, 69.1, 51.5, 26.5, and 20.6. Anal. Calcd for $C_{19}H_{20}O_6S_2$: C, 55.93; H, 4.94; S, 15.72. Found: C, 56.10; H, 4.89; S, 16.01.

(*S*)-1-(Phenylsulfonyl)-3-pentanol [(*S*)-3a]. A solution of 456 mg of (±)-**3a** (2.0 mmol) in 40 mL of $^iPr_2O$ was acetylated for 3.5 h. A total of 280 mg of (*R*)-**4a** (52%) and 205 mg of (*S*)-**3a** (45%) was obtained (hexane–ethyl acetate (3:1)). Ee: 92%. $[\alpha]^{25}_D$: +23.0 (c = 1, $CHCl_3$). IR ($CHCl_3$): 3450, 1435, 1295, 1135, and 1075 cm^{-1}. ^{1}H-NMR δ: 7.92 (m, 2 H, $PhSO_2$), 7.61 (m, 3 H, $PhSO_2$), 3.63 (m, 1 H, C*H*OH), 3.27 (m, 2 H, CH_2OH), 1.98 (m, 1 H, CH_2CH_2S), 1.75 (m, 1 H, CH_2CH_2S), 1.73 (br s, 1 H, OH), 1.47 (m, 2 H, CH_2CH_3), and 0.93 (t, 3 H, J = 7.4 Hz, CH_3). ^{13}C-NMR δ: 138.7, 133.6, 129.1, 127.7, 70.8, 52.8, 29.9, 29.1, and 9.6. Anal. Calcd for $C_{11}H_{16}O_3S$: C, 57.94; H, 7.07; S, 14.06. Found: C, 58.10; H, 6.87; S, 14.24.

Acetate (*R*)-4a. Ee: 81%. $[\alpha]^{25}_D$: +12.3 (c = 1, $CHCl_3$). IR ($CHCl_3$): 1725, 1230, 1135, and 1075 cm^{-1}. ^{1}H-NMR δ: 7.92 (m, 2 H, $PhSO_2$), 7.63 (m, 3 H, $PhSO_2$), 4.81 (m, 1 H, C*H*OAc), 3.11 (m, 2 H, CH_2OH), 2.01 (s, 3 H, CH_3CO_2), 1.98 (m, 2 H, CH_2CH_2S), 1.55 (m, 2 H, CH_2CH_3), and 0.86 (t, 3 H, J = 7.4 Hz, CH_3). ^{13}C-NMR δ: 170.3, 138.6, 133.6, 129.1, 127.7, 72.9, 52.4, 26.6, 26.3, 20.7, and 9.1. Anal. Calcd for $C_{13}H_{18}O_4S$: C, 57.82; H, 6.72; S, 11.87. Found: C, 57.85; H, 6.49; S, 11.53.

(*R*)-4-Methyl-1-(phenylsulfonyl)-3-pentanol [(*R*)-3b]. A solution of 242 mg of (±)-**3b** (1.0 mmol) in 20 mL of $^iPr_2O$ was acetylated for 14 days. A total of 133 mg of (*S*)-**4b** (47%) and 116 mg of alcohol (*R*)-**3b** (48%) was obtained (hexane–ethyl acetate (2:1)). Ee: 53%. $[\alpha]^{25}_D$: +12.4 (c = 1, $CHCl_3$). IR ($CHCl_3$): 3450, 2950, 1435, 1295, 1135, and 1075 cm^{-1}. ^{1}H-NMR δ: 7.92 (m, 2 H, $PhSO_2$), 7.63 (m, 3 H, $PhSO_2$), 3.47–3.11 (m, 3 H, C*H*OH and CH_2SO_2), 2.03–1.54 (m, 3 H, C*H*CH_3 and CH_2CH_2S), 1.78 (br s, 1 H, OH), 0.91 (d, 3 H, J = 6.7 Hz, CH_3CH), and 0.88 (d, 3 H, J = 6.7 Hz, CH_3CH). ^{13}C-NMR δ: 138.7, 133.5, 129.1, 127.7, 74.4, 53.2, 33.6, 26.6, 18.2, and 17.3.

Acetate (*S*)-4b. Ee: 52%. $[\alpha]^{25}_D$: +2.5 (c = 1, $CHCl_3$). ^{1}H-NMR δ: 7.90 (m, 2 H, $PhSO_2$), 7.63 (m, 3 H, $PhSO_2$), 4.70 (m, 1 H, C*H*OAc), 3.07 (m, 2 H, CH_2SO_2), 2.02 (s, 3 H, CH_3CO_2), 2.00 (m, 2 H, CH_2CH_2S), 1.77 (m, 1 H, CH), 0.87 (d, 3 H, J = 6.8 Hz, CH_3), and 0.86 (d, 3 H, J = 6.8 Hz, CH_3). ^{13}C-NMR δ: 170.6, 138.5, 133.6, 129.1, 127.7, 76.1, 52.6, 31.1, 24.0, 20.6, 17.8, and 17.4. Anal. Calcd for $C_{14}H_{20}O_4S$: C, 59.16; H, 7.09; S, 11.28. Found: C, 59.05; H, 7.20; S, 11.32.

(2*R*,3*R*)-2-Methyl-1-(phenylsulfonyl)-3-pentanol [(2*R*,3*S*)-3c]. A solution of 242 mg of (±)-**3c** (1.0 mmol) in 20 mL of $^iPr_2O$ was acetylated for 96 h. A total of 130 mg of (2*S*,3*R*)-**4c** (46%) and 106 mg of (2*R*,3*S*)-**3c** (44%) was obtained (hexane–ethyl acetate (3:1)). Ee: 91%. $[\alpha]^{25}_D$: +1.3 (c = 1, $CHCl_3$). IR ($CHCl_3$): 3490, 2940, 1435, 1290, 1135, and 1075 cm^{-1}. ^{1}H-NMR δ: 7.92 (m, 2 H, $PhSO_2$), 7.61 (m, 3 H, $PhSO_2$), 3.70 (ddd, 1 H, J = 8.2, 5.4, and 3.0 Hz, C*H*OH), 3.66 (dd, 1 H, J = 14.0 and 5.9 Hz, CH_2SO_2), 2.97 (dd, 1 H, J = 14.1 and 6.8 Hz, CH_2SO_2), 2.32 (m, 1 H, CH), 1.72 (br s, 1 H, OH), 1.43 (m, 2 H, CH_2CH_3), 1.02 (d, 3 H, J = 7.0 Hz, CH_3CH), and 0.95 (t, 3 H, J = 7.4 Hz, CH_3CH_2). ^{13}C-NMR δ: 139.8, 133.6, 129.2, 127.6, 74.7, 59.4, 33.3, 26.3, 13.5, and 10.5.

Acetate (2*S*,3*R*)-4c. Ee: 84%. $[\alpha]^{25}_D$: +29.8 (c = 1, $CHCl_3$). IR ($CHCl_3$): 2950, 1710, 1295, 1225, 1135, and 1075 cm^{-1}. ^{1}H-NMR δ: 7.92 (m, 2 H, $PhSO_2$), 7.62 (m, 3 H, $PhSO_2$), 4.71 (ddd, 1 H, J = 8.2, 5.7, and 3.4 Hz, C*H*OAc), 3.22 (dd, 1 H, J = 14.1 and 2.9 Hz, CH_2S), 2.89 (dd, 1 H, J = 14.1 and 9.0 Hz, CH_2S), 2.38 (m, 1 H, C*H*CH_3), 1.95 (s, 3 H, CH_3CO_2), 1.49 (m, 2 H, CH_2CH_3), 1.12 (d, 3 H, J = 6.9 Hz, CH_3CH), and 0.84 (t, 3 H, J = 7.4 Hz, CH_2CH_3). ^{13}C-NMR δ: 170.6, 139.6, 133.7, 129.3, 127.9, 77.6, 59.1, 31.5, 23.2, 20.9, 14.6, and 10.0.

(*S*)-3-(Methoxymethoxy)-1-(trimethylsilyl)-1-(phenylsulfonyl)-1-penten-3-ol [(*S*)-6]. To a solution of the alcohol (*S*)-**1b** (1.11 g, 4.9 mmol) in $CHCl_3$ (50 mL) were added 8.67 mL of dimethoxymethane and 14 g of P_2O_5. The solution was stirred for 2 h at rt. The reaction was cooled at 0 °C, and a saturated solution of aqueous Na_2CO_3 (50 mL) was added. The organic layer was separated, and the aqueous layer was extracted with ether (2 × 50 mL). The combined organic layers were dried (Na_2SO_4) and evaporated. The residue was purified by chromatography (hexane–ethyl acetate (4:1)) to afford 1.21 g (92% yield) of MOM-(*S*)-**1b**. $[\alpha]^{25}_D$: −30.5 (c = 1, $CHCl_3$). ^{1}H-NMR δ: 7.89 (m, 2 H, $PhSO_2$), 7.58 (m, 3 H, $PhSO_2$), 6.91 (dd, 1 H, J = 15.0 and 5.2 Hz, C*H*=CHS), 6.53 (dd, 1 H, J = 15.0 and 1.4 Hz, CH=C*H*S), 4.58 (m, 2 H, OCH_2O), 4.20 (m, 1 H, C*H*O), 3.32 (s, 3 H, CH_3O), 1.65 (m, 2 H, CH_2CH_3), and 0.92 (t, 3 H, J = 7.3 Hz, CH_3CH_2). ^{13}C-NMR δ: 145.9, 140.2, 133.4, 130.8, 129.3, 127.5, 95.0, 75.6, 55.6, 27.4, and 9.2. MS: 241 (M^+ - 29), 211 (26), 129

(49), 125 (85), 99 (32), 97 (35), 77 (100). Anal. Calcd for $C_{13}H_{18}O_4S$: C, 57.82; H, 6.72; S, 11.87. Found: C, 57.62; H, 6.51; S, 11.71. A solution 3.5 M of ^nBuLi in hexane (1.2 mL, 4.2 mmol) was slowly added to a solution of MOM-(*S*)-**1b** (1.14 g, 4.2 mmol) in dry THF (50 mL) at −78 °C under argon. The solution was kept at −78 °C for 20 min and at 0 °C for 30 min. The solution was cooled again at −78 °C, and 2.14 mL (16.9 mmol) of trimethylsilyl chloride was added. After 1 h of reaction a saturated solution of aqueous NH_4Cl (50 mL) was added. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were dried (Na_2SO_4) and evaporated. The residue was purified by chromatography (hexane–ethyl acetate (8:1)) to afford 1.26 g (87% yield) of (*S*)-**6**. $[\alpha]^{25}_D$: −63.8 (*c* = 1, $CHCl_3$). ^{1}H-NMR δ: 7.80 (m, 2 H, $PhSO_2$), 7.55 (m, 3 H, $PhSO_2$), 7.23 (d, 1 H, *J* = 9.6 Hz, CH=C), 4.61 (m, 2 H, OCH_2O), 4.39 (m, 1 H, C*H*O), 3.38 (s, 3 H, CH_3O), 1.60 (m, 2 H, CH_2CH_3), 1.02 (t, 3 H, *J* = 7.4 Hz, CH_3CH_2), and 0.20 (s, 9 H, $(CH_3)_3Si$). ^{13}C-NMR δ: 157.0, 144.3, 140.9, 132.4, 128.5, 126.9, 94.3, 74.5, 54.9, 27.7, 9.2, and 0.3. MS: 313 (M^+ − 29), 297 (100), 283 (26), 265 (22), 135 (82), 125 (39), 77 (31). Anal. Calcd for $C_{16}H_{26}O_4SSi$: C, 56.15; H, 7.65; S, 9.36. Found: C, 56.44; H, 7.60; S, 9.15.

(2*R*,3*S*)-3-(Methoxymethoxy)-2-methyl-1-(phenylsulfonyl)pentane [(2*R*,3*S*)-7]. MeLi (1.6 M) in Et_2O (2.6 mL, 4.1 mmol) was slowly added to a solution of (*S*)-**6** (1.09 g, 3.2 mmol) in Et_2O (25 mL) at −78 °C under argon. The solution was kept at −78 °C for 30 min. Then, a saturated solution of aqueous NH_4Cl (50 mL) was added. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were dried (Na_2SO_4) and evaporated. The residue was dissolved in MeOH (25 mL), and 1.75 g of KF was added. The reaction was stirred at rt, for 1 h. Water was added, and the resulting solution was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were dried (Na_2SO_4) and evaporated. The residue was purified by chromatography (hexane–ethyl acetate (5:1)) to afford 783 mg (92% yield) of (2*R*,3*S*)-7. $[\alpha]^{25}_D$: −36.2 (*c* = 1, $CHCl_3$). ^{1}H-NMR δ: 7.93 (m, 2 H, $PhSO_2$), 7.60 (m, 3 H, $PhSO_2$), 4.49 (m, 2 H, OCH_2O), 3.41 (m, 1 H, CHO), 3.40 (dd, 1 H, *J* = 14.1 and 3.5 Hz, CH_2SO_2), 3.29 (s, 3 H, CH_3O), 2.90 (dd, 1 H, *J* = 14.4 and 8.6 Hz, CH_2SO_2), 2.38 (m, 1 H, C*H*CH_3), 1.40 (m, 2 H, CH_2CH_3), 1.07 (d, 3 H, *J* = 7.0 Hz, C*H*$_3$CH), and 0.88 (t, 3 H, *J* = 7.4 Hz, CH_3CH_2). ^{13}C-NMR δ: 139.4, 132.9, 128.6, 127.2, 95.1, 81.0, 57.9, 54.8, 30.5, 22.7, 14.2, and 9.8. Anal. Calcd for $C_{14}H_{22}O_4S$: C, 58.71; H, 7.74; S, 11.20. Found: C, 58.60; H, 7.35; S, 11.15.

(3*S*,4*R*,5*R*)- and (3*S*,4*R*,5*S*)-4-Methyl-5-(phenylsulfonyl)-3-heptanol (8). A solution 3.5 M ^{n}BuLi in hexane (0.81 mL, 2.85 mmol) was slowly added to a solution of (2*R*,3*S*)-7 (740 mg, 2.59 mmol) in THF–HMPA (4:1) (50 mL) at −78 °C under argon atmosphere. The solution was kept at −78 °C for 30 min. A total of 0.84 mL (10 mmol) of ethyl iodide was added, and the reaction was allowed to stand at rt. After 24 h at rt a saturated solution of aqueous NH_4Cl (50 mL) was added. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were dried (Na_2SO_4) and evaporated. The residue was dissolved in THF (50 mL), and 6 M HCl (30 mL) was added. The mixture was stirred at room temperature for 5 h. Then, a saturated solution of aqueous $NaHCO_3$ (20 mL) was added, the organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were dried (Na_2SO_4) and evaporated. The residue was purified by chromatography (hexane–ethyl acetate (4:1)) to afford 613 mg (88% yield) of sulfones 8 as a 5:1 mixture of both epimers at C-5. $[\alpha]^{25}_D$: +4.5 (*c* = 1, $CHCl_3$). ^{1}H-NMR δ: 7.90 (m, 2 H, $PhSO_2$), 7.63 (m, 3 H, $PhSO_2$), 3.90 and 3.67 (m, 1 H, C*H*OH), 3.06 and 2.98 (m, 1 H, C*H*SO_2Ph), 2.31 (m, 1 H, $CHCH_3$), 1.80 (m, 2 H, CH_2CHOH), 1.40 (m, 2 H, CH_2CHSO_2), 1.20 and 1.01 (d, 3 H, *J* = 7.2 Hz, C*H*$_3$CH), 0.98 (t, 3 H, *J* = 7.3 Hz, CH_3CH_2), and 0.84 (t, 3 H, *J* = 7.3 Hz, C*H*$_3$CH$_2$). ^{13}C-NMR δ: 139.0, 133.5, 129.2, 128.6 (128.4), 75.3 (75.0), 68.4 (71.3), 36.9 (38.1), 27.4 (28.8), 19.1 (20.6), 12.8 (12.3), 10.3 (10.6), and 9.8 (9.5). Anal. Calcd for $C_{14}H_{22}O_3S$: C, 62.19; H, 8.20; S, 11.86. Found: C, 62.21; H, 8.35; S, 11.70.

(3*S*,4*S*)-4-Methyl-3-heptanol (9). To a mixture of sulfones 8 (550 mg, 2.0 mmol) and anhydrous Na_2HPO_4 (1.16 g, 8.0 mmol) in 5 mL of dry MeOH was added 3.0 g of pulverized 6% sodium amalgam. The solution was vigorously stirred at rt for 6 h, and then the reaction was poured into water and extracted with ether (2 × 50 mL). The combined organic layers were dried (Na_2SO_4) and evaporated. The residue was distilled to afford 213 mg of (3*S*,4*S*)-**9** (80% yield). Bp: 110–115 °C (100 mm). $[\alpha]^{25}_D$: −23.0 (*c* = 1, hexane) (lit.[20] $[\alpha]^{25}_D$ −21.7 (hexane)).

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Registry No. (±)-**1a**, 137764-78-4; (±)-**1b**, 137653-98-6; (±)-**1c**, 137653-99-7; (±)-**1d**, 141088-31-5; (±)-**1e**, 137764-79-5; (±)-**1f**, 141117-91-1; (±)-**1g**, 137654-00-3; (±)-**1h**, 141088-32-6; (±)-**1i**, 141195-85-9; (*S*)-**1a**, 132016-57-0; (*S*)-**1b**, 137764-80-8; (*S*)-**1c**, 137764-81-9; (*S*)-**1d**, 141195-86-0; (*S*)-**1e**, 132016-59-2; (*S*)-**1g**, 137764-82-0; (*S*)-**1h**, 141195-87-1; (*R*)-**2a**, 141088-33-7; (*R*)-**2b**, 141088-34-8; (*R*)-**2c**, 141088-35-9; (*R*)-**2d**, 141088-36-0; (*R*)-**2e**, 141195-88-2; (*R*)-**2g**, 141088-37-1; (*R*)-**2h**, 141088-38-2; (±)-**3a**, 141195-89-3; (±)-**3b**, 141088-39-3; (±)-**3c**, 141195-90-6; (*S*)-**3a**, 131701-89-8; (*R*)-**3b**, 141195-91-7; (2*R*,3*S*)-**3c**, 137654-02-5; (*R*)-**4a**, 141088-40-6; (*S*)-**4b**, 141088-41-7; (2*S*,3*R*)-**4c**, 141088-42-8; AcO-CH=CH_2, 108-05-4; lipase PS, 9001-62-1.