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Remote Stereocontrol by Sulfinyl Groups: Reduction of δ-Ketosulfoxides

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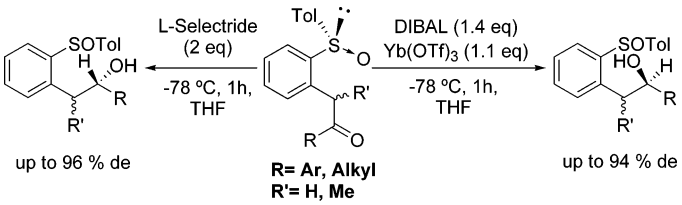

The reduction of δ-ketosulfoxides constitutes the first evidence of the efficiency of the sulfinyl group to control the stereoselectivity of 1,5-asymmetric induction processes. The use of DIBAL/$Yb(OTf)_3$ or L-Selectride as the reducing agents provides δ-hydroxysulfoxides with the opposite configuration at the hydroxylic carbon in a highly stereoselective way.

1. Introduction

Conformational restrictions are in the origin of the stereodifferentiation of the prochiral centers required in any asymmetric process. When these are close to the chiral auxiliary responsible for the asymmetric induction, there are several plausible mechanisms controlling the conformational preferences, many of them involving direct interactions (steric and/or electronic) between them. This makes the stereoselectivity control easier. The longer the distance is between the inductor and the prochiral center the smaller the capability of the former one to restrict the conformations around the prochiral center, thus decreasing their efficiency as inductor. Thus, the remote stereocontrol is one of the most intriguing challenges to be solved in asymmetric synthesis.[1,2]

One of the most frequently used strategies to get prochiral centers and chiral inducers close to each other involves the use of Li^+ as a Lewis acid to form chelated species.[2] Consequently, these groups used to get the remote stereocontrol usually have basic centers prone to interact with such a Lewis acid. The high affinity of the sulfinyl oxygen toward different Lewis acids has been evidenced in many 1,2- and 1,3-asymmetric induction processes.[3] By contrast, reactions with a longer distance between the prochiral center and the sulfur atom have been much less studied. This was the reason we initiated a program to investigate the ability of the sulfinyl group to control the stereoselectivity of reactions taking place at remote positions ($1 - n$ asymmetric induction processes with $n > 3$). In this context we have recently reported several papers concerning reactions of γ-sulfinyl carbanions with different electrophiles[4] (nucleophilic 1,4-asymmetric induction processes) showing the high efficiency of the sulfinyl group. Additionally, other authors had shown that it was also the case for reactions of nucleophiles with 2-sulfinyl derivatives of aromatic aldehydes[5] (electrophilic 1,4-asymmetric induction processes). However, to our knowledge, there has not been reported to date any highly stereoselective reaction controlled by sulfinyl groups located farther from the reaction center.[6]

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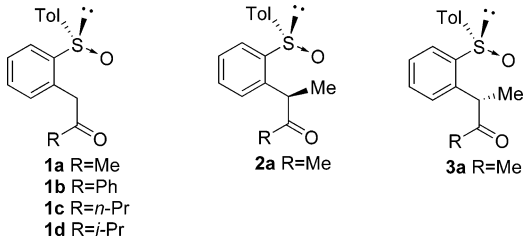
SCHEME 1



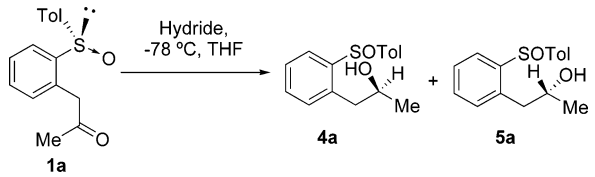
The face-selectivity for the reductions of carbonyl compounds mediated by chiral sulfoxides has been intensively studied in β-ketosulfoxides[7] (1,3-induction). Particularly, their reduction with diisobutylaluminum hydride (DIBAL) giving β-hydroxysulfoxides proceeded with high diastereoselectivity through a six-membered cyclic transition state.[7b] The number of reports concerning reduction of γ-ketosulfoxides (1,4-induction) is much lower;[8] the best results have been reported by Solladié[9] and Toru.[10] We present herein the first results concerning the stereoselective reduction of δ-ketosulfoxides (1,5-induction), which demonstrate the ability of the sulfinyl group in the remote control of the stereoselectivity.

2. Results and Discussion

As the starting compounds we have used the 1-alkyl (or phenyl) 2-(2-*p*-tolylsulfinyl)phenyl ethanones, **1a**−**d**, and the epimers at C-2 of the methyl derivatives, **2a** and **3a** (Scheme 1). The synthesis of all these compounds has been reported recently.[4f]

We first investigated the reduction of **1a** under different conditions (Table 1). The use of DIBAL did not give good stereochemical results and a 43:57 mixture of epimers **4a** and **5a** was obtained in high yield (entry 1). This low stereoselectivity could not be significantly increased by using either $ZnCl_2$ (which only slightly inverts the sense of the stereoselectivity, entry 2) or other Lewis acids ($CeCl_3$, $Ti(OiPr)_4$, and LiBr, entries 3−5) as the catalysts, and the reaction did not work at all in the presence of $Sn(OTf)_3$ (entry 6). Fortunately, the reaction conducted in the presence of $Yb(OTf)_3$ afforded a 97:3 diastereomeric ratio of epimers, which allowed the isolation of diastereomerically pure **4a** by ready flash chromatography in 89% yield (entry 7). Finally, we investigated the behavior of other hydrides. The only relevant results were obtained with L-Selectride. With this reagent, a 5:95 mixture of **4a**:**5a** was obtained (entry 8) in 75% yield (71% of pure **5a**), therefore affording a complete inversion of the stereoselectivity.

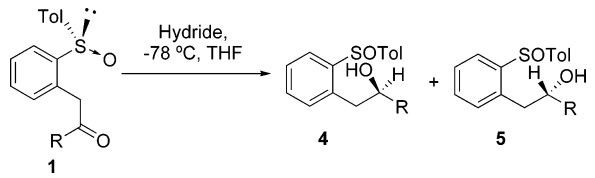
TABLE 1. Reaction of 1a under Different Reduction Conditions



entry	hydride	Lewis acid	**4a**:**5a**	yield (%)
1	DIBAL		43:57	97
2	DIBAL	$ZnCl_2$	61:39	96
3	DIBAL	$CeCl_3$	39:61	94
4	DIBAL	$Ti(OiPr)_4$	58:42	95
5	DIBAL	LiBr	61:49	96
6	DIBAL	$Sn(OTf)_3$		
7	**DIBAL**	**$Yb(OTf)_3$**	**97**[a]**:3**	**96**
8	**L-Selectride**		**5**:**95**[b]	**75**

[a] Isolated yield 89%. [b] Isolated yield 71%.

TABLE 2. Reduction of Compounds 1b−d



entry	substrate	hydride/LA	**4**:**5**	yield (%)
1	**1b** (R = Ph)	DIBAL	33:67	96
2	**1b** (R = Ph)	DIBAL/LA[a]	89[b]:11	95
3	**1b** (R = Ph)	L-Selectride	40:60	55
4	**1c** (R = *n*-Pr)	DIBAL	84:16	96
5	**1c** (R = *n*-Pr)	DIBAL/LA[a]	92[c]:8	95
6	**1c** (R = *n*-Pr)	L-Selectride	2:98[d]	65
7	**1d** (R = *i*-Pr)	DIBAL	58:42	95
8	**1d** (R = *i*-Pr)	DIBAL/LA[a]	92[e]:8	97
9	**1d** (R = *i*-Pr)	L-Selectride	2:98[f]	60

[a] $Yb(OTf)_3$. [b] Isolated yield 83%. [c] Isolated yield 90%. [d] Isolated yield 61%. [e] Isolated yield 91%. [f] It is obtained with **1d**.

We next tried the reduction of ketosulfoxides **1b**−**d** under the best conditions indicated in Table 1. The results are reported in Table 2.

The stereoselectivity observed in DIBAL reductions was not good in any case, yielding mixtures of the epimeric alcohols **4** and **5**. By contrast, reactions with DIBAL/$Yb(OTf)_3$ or L-Selectride evolved in an opposite and highly stereoselective manner, yielding alcohols **4** and **5** which could be easily purified by chromatography from the mixtures where they were the major products. The only exception was observed for **1b** in the reduction with L-Selectride (entry 3), which afforded a 40:60 mixture of epimers, hence preventing an easy purification of **5b**. Yields were almost quantitative with DIBAL/$Yb(OTf)_3$ but only 55−75% with L-Selectride.

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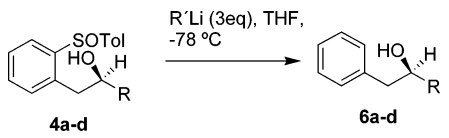
TABLE 3. Desulfinylation of Compounds 4



entry	substrate	R'Li	yield (%)
1	**4a** (R = Me)	*t*-Bu	**6a** (67)
2	**4b** (R = Ph)	*n*-Bu	**6b** (60)
3	**4c** (R = *n*-Pr)	*t*-Bu	**6c** (54)
4	**4d** (R = *i*-Pr)	*n*-Bu	**6d** (70)

Configurational assignment of the hydroxysulfoxides **4a**−**d** was performed by chemical correlations with the previously reported alcohols **6a**−**d**.[11] The reactions of the hydroxysulfoxides with alkyllithium reagents, under the conditions collected in Table 3, yielded the alcohols **6**.[12]

These correlations allowed us to assign the configuration of the carbinols according to those indicated in Table 3 (*R* for **4b** and **4d** and *S* for **4a** and **4c**). As the configuration at sulfur for all compounds **4** must be *S* (identical with that of the starting ketones **1**), these correlations provided the absolute configurations for **4** and **5** (epimers at the hydroxylic carbon).

The results collected in Tables 1 and 2 suggest that the sulfinyl group is efficient to control the stereoselectivity of the reduction of δ-ketosulfoxides (1,5-asymmetric induction) by using the proper conditions. The high stereoselectivity observed in those reactions with nucleophilic hydrides such as L-Selectride suggests that the sulfinyl group is able to restrict the conformational mobility differentiating the two diastereotopic faces of the carbonyl group. Figure 1 depicts the presumably most stable conformations, **A** and **B**, for compounds **1a**−**d**. They exhibit the lone electron pair at sulfur oriented toward the benzylic carbon. Additionally, the COR group adopts the orthogonal arrangement with respect to the aromatic ring, thus minimizing the allylic strain. Finally, the anti relationship between the Ar and R groups around the CH_2−CO bond could also be favored by steric grounds. The conformational equilibrium must be shifted toward the **A** conformers because the electrostatic repulsion between the sulfinyl and carbonyl oxygens decreases the stability of the **B** ones. By assuming that the attack of the nucleophilic hydrides will be mainly controlled by steric grounds, the favored approach of the bulky L-Selectride will take place from the bottom face, resulting in the formation of **5** as the major alcohols. The smaller size of DIBAL and mainly its ability to associate with the sulfinyl oxygen as a previous step to its intramolecular attack to the upper face of **A** conformers could be invoked to justify the poorer face selectivity observed for DIBAL reductions. The strong capability of the $Yb(OTf)_3$ to associate with the oxygen determines the formation of the chelated species **C** and **D**, the latter one being the most stable due to steric reasons. The attack of the

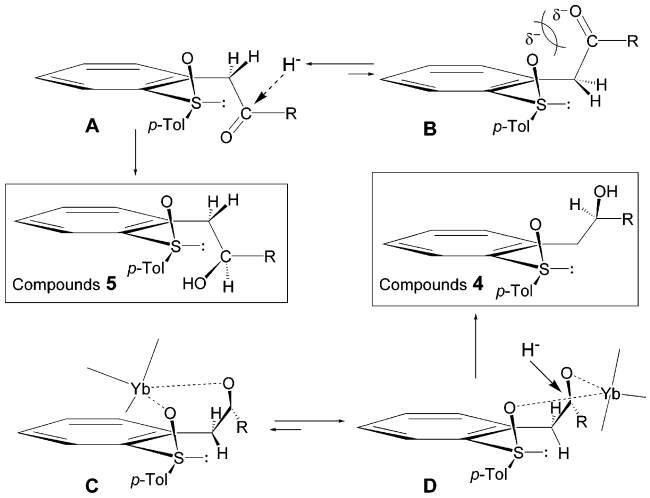


FIGURE 1. Favored conformations accounting for the observed stereoselectivity.

hydride to the less hindered face of **D**[13] accounts for the formation of alcohols **4** as the major products (Figure 1).

With the aim of establishing the influence of an additional stereogenic center on the stereoselectivity, as well as the competition between both chiral centers, we have also studied the behavior of **2a** and **3a**, the two α-methyl derivatives of **1a**. The synthesis of these compounds as well as their configurational assignment had been previously reported.[4f] The results obtained in their reduction with different hydrides are collected in Table 4.

Compound **3a** did not evolve stereoselectively under any of the studied reaction conditions (≈1:1 mixtures of **9a** and **10a** were obtained in all cases). By contrast, **2a** evolved with a complete control of the stereoselectivity in its reaction with DIBAL/$Yb(OTf)_3$, which makes easy the synthesis of **7a**. Under different conditions (DIBAL or L-Selectride), mixtures of **7a** and **8a** were obtained. In all cases the diastereisomers could be separated and purified by flash chromatography. These results are consistent with the stereochemical model indicated in Figure 1. The presence of the methyl group at the benzylic position must play a significant role in the composition of the conformational equilibria. Its interactions with the sulfinyl oxygen in one diastereoisomer or with H_{ortho} in the other epimer would destabilize the conformations **A** in Figure 1. This fact would determine that several conformations have a significant population, whose evolution with DIBAL or L-Selectride would explain the formation of both epimeric alcohols with the consequent decrease in stereoselectivity. In the presence of $Yb(OTf)_3$, the stability of the chelated species **D** (Figure 2) will depend on the configuration of the methyl derivative. It will be stable for **2a** but not for **3a** due to the steric repulsion of the methyl group with the substituents joined to Yb (Figure 2). As a consequence, only **2a** will be able to evolve in a completely stereoselective way into **7a**, according to the approach of the DIBAL to the less hindered face of the chelated substrate.

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(12) The compounds resulting from the nucleophilic substitution of the *p*-tolyl group by the alkyl group of the lithium reagent were also obtained as nondesired byproducts.

(13) The approach of the DIBAL to the opposite face, which would yield compounds **4**, is hindered by the substituents at Yb.

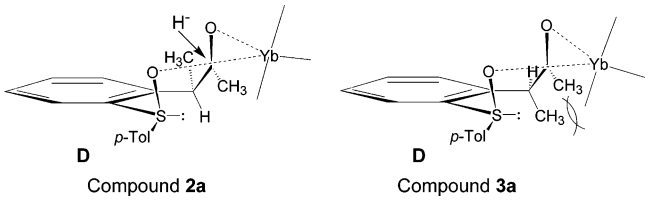
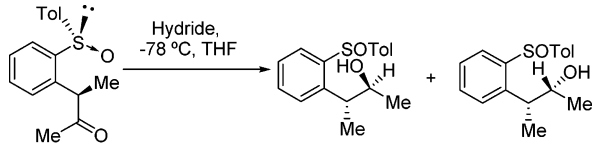


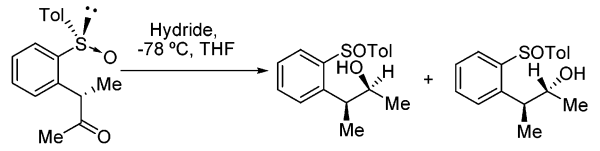
FIGURE 2. Chelated species for **2a** and **3a**.

TABLE 4. Reduction of γ-Methyl-δ-ketosulfoxides 2a and 3a



2a **7a** **8a**

Hydride	**7a** : **8a**	Yield (%)
DIBAL	42 : 58	74
DIBAL/Yb(OTf)$_3$	100 : 0	70
L-Selectride	86 : 14	65



3a **9a** **10a**

Hydride	**9a** : **10a**	Yield (%)
DIBAL	58 : 42	87
DIBAL/Yb(OTf)$_3$	56 : 44	94
L-Selectride	53 : 47	60

The configurational assignment of compounds **7a**−**10a** was based on the assumption that their configurations at sulfur and benzylic carbon must be identical with those of their respective precursors **2a** [3*R*,(S)*S*] and **3a** [3*S*,(S)*S*], which had been previously assigned.[4f] Thus, it was only necessary to determine their configurations at the hydroxylic carbon. It was unequivocally established as *S* for compound **7a**, from its chemical correlation with compound **11** (Scheme 2), previously reported in the literature.[14] Additionally, the individual oxidation of **7a** and **10a** with MCPBA yielded the enantiomers **12** and *ent*-**12**, respectively, thus allowing us to assign the configuration of **10a** as *R* at its hydroxylic carbon (Scheme 2). The absolute configurations of the other two compounds, **8a** and **9a**, were assigned as indicated in Table 4, considering that they are epimers of **7a** and **10a**, respectively, at the hydroxylic carbon.

As a conclusion, we have provided the first evidence of the efficiency of the sulfinyl group as a chiral inductor in the reduction of carbonyl groups separated by 4 bonds from the chiral sulfur (1,5-asymmetric induction). The use of large hydrides or Lewis acids such as Yb(OTf)$_3$

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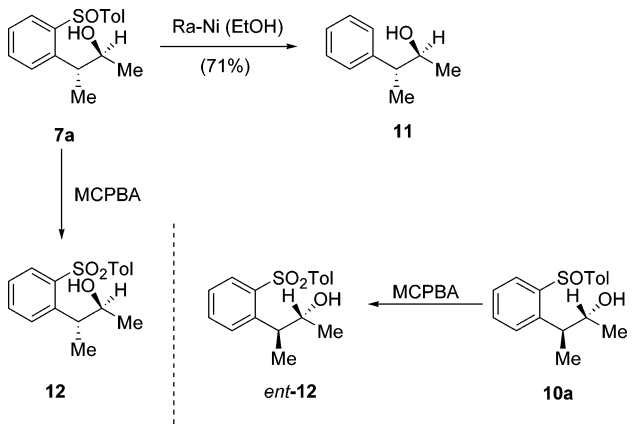
SCHEME 2



provides a stereodivergent route to prepare alcohols with the two possible configurations. Only one of the epimers resulting from the methylation at C-α is able to evolve in a completely stereoselective way. The results of the reactions with other nucleophiles will be published in due course.

3. Experimental Section

Method A: Reduction with DIBAL. General Procedure. To a solution of sulfoxide **1** (0.14 mmol) in 3 mL of THF cooled at −78 °C was added a mixture of 0.2 mL (0.20 mmol) of a 1 M solution of DIBAL in heptane (in the case of **1d**, the addition of three portions of 0.29 mmol of the hydride was necessary). The resulting solution was stirred for 1 h and the mixture was quenched with 1.5 mL of methanol. The solvent was evaporated in vacuo, and the residue was diluted with 10% HCl, extracted with CH_2Cl_2 (3 × 3 mL), and dried ($MgSO_4$) and the solvent was evaporated. The residue was purified by flash-column chromatography.

Method B: Reduction with DIBAL/Lewis Acid. General Procedure. A solution of sulfoxide **1** (0.14 mmol) and Lewis acid (0.15 mmol) in 3 mL of THF was stirred at room temperature for 30 min. Then, 0.2 mL (0.2 mmol) of a 1 M solution of DIBAL in heptane was added to the cooled (−78 °C) solution (in the case of **2a** and **3a**, the addition of three portions of 0.29 mmol of the hydride was necessary). The resulting mixture was stirred for 1 h and quenched, extracted, and purified as in method A.

Method C: Reduction with L-Selectride. General Procedure. To a solution of sulfoxide **1** (0.14 mmol) in 3 mL of THF cooled at −78 °C was added 0.2 mL (0.28 mmol) of a 1 M solution of l-Selectride in THF. The resulting solution was stirred for 1 h and the mixture was quenched with 1.5 mL of 1 M HCl, extracted with CH_2Cl_2 (3 × 3 mL), and dried ($MgSO_4$) and the solvent was evaporated. The residue was filtered over Celite and purified by flash-column chromatography.

[2*S*,(S)*S*]-1-[2-(*p*-Tolylsulfinyl)phenyl]propan-2-ol (4a). **4a** was isolated diastereomerically pure by flash-column chromatography (AcOEt−hexane 1:1) of the crude mixture **4a** + **5a**. Yield 89% (method B), gummy; $[\alpha]^{20}_D$ −55.0 (*c* 0.5, $CHCl_3$); IR (film) 3395, 1083, 810 cm^{-1}; ^{1}H NMR δ 7.75−7.72 (m, 1H), 7.44−7.34 (m, 4H), 7.26−7.18 (m, 3H), 3.93 (br s, 1H), 2.90 (d, *J* = 6.1 Hz, 2H), 2.32 (s, 3H), 1.15 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR δ 143.5, 141.5, 141.0, 137.5, 131.3, 131.1, 129.9, 127.5, 125.8, 125.7, 67.6, 41.0, 22.9, 21.2; MS (EI) *m/z* 257 [M$^+$ − H_2O]; HRMS [M$^+$ − H] calcd for $C_{16}H_{17}O_2S$ 273.0949, found 273.0952.

[2*R*,(S)*S*]-1-[2-(*p*-Tolylsulfinyl)phenyl]propan-2-ol (5a). **5a** was isolated diastereomerically pure by flash-column chromatography (AcOEt−hexane 1:1) of the crude mixture **4a** + **5a**. Yield 71% (method C), gummy; $[\alpha]^{20}_D$ −105.6 (*c* 1.1, $CHCl_3$); ^{1}H NMR δ 7.74−7.71 (m, 1H), 7.40−7.15 (m, 7H), 3.93 (m, 1H), 2.84 (dd, *J* = 13.7 and 8.1 Hz, 1H), 2.76 (dd, *J* = 13.7

and 4.9 Hz, 1H), 2.50 (br s, 1H), 2.29 (s, 3H), 1.21 (d, J = 6.0 Hz, 3H); ^{13}C NMR δ 143.3, 141.3, 141.2, 138.6, 131.6, 131.5, 129.9, 127.5, 127.0, 125.4, 68.7, 41.2, 23.9, 21.3.

[1*R*,(S)*S*]-1-Phenyl-2-[2-(*p*-tolylsulfinyl)phenyl]ethanol (4b). 4b was isolated diastereomerically pure by flash-column chromatography (AcOEt−hexane 1:1) of the crude mixture **4b** + **5b**. Yield 83% (method B); white solid; mp 80−82 °C; $[\alpha]^{20}_D$ −62.7 (*c* 1.0, $CHCl_3$); IR (film) 3357, 1594, 1082 cm^{-1}; ^{1}H NMR δ 7.67−7.64 (m, 1H), 7.41−7.02 (m, 11H), 7.05−7.02 (m, 1H), 4.80 (dt, J = 6.1 and 3.6 Hz, 1H), 3.42 (br d, J = 3.6 Hz, OH), 3.13 (d, J = 6.1 Hz, 2H), 2.36 (s, 3H); ^{13}C NMR δ 143.7, 143.5, 141.4, 140.7, 137.2, 131.7, 131.0, 129.9, 128.2, 127.5, 127.4, 126.2, 125.8, 125.7, 73.9, 41.4, 21.3; MS (EI) *m/z* 319 [M − 17]$^+$; HRMS [M + 1]$^+$ calcd for $C_{21}H_{21}O_2S$ 337.1262, found 337.1261.

[1*S*,(S)*S*]-1-Phenyl-2-[2-(*p*-tolylsulfinyl)phenyl]ethanol (5b). 5b could not be isolated diastereomerically pure. It was characterized from a mixture of **4b** + **5b** obtained by flash-column chromatography (AcOEt−hexane 1:1); ^{1}H NMR (representative parameters) δ 7.80−7.77 (m, 1H), 4.74 (m, 1H), 3.14 (dd, J = 14.1 and 9.7 Hz), 2.87 (dd, J = 14.1 and 4.0 Hz), 2.26 (s, 3H); ^{13}C NMR (representative parameters) δ 144.6, 143.6, 141.1, 141.0, 138.5, 132.0, 131.8, 129.8, 128.6, 128.4, 127.5, 127.3, 125.6, 125.1, 74.9, 41.6, 21.2.

[2*S*,(S)*S*]-1-[2-(*p*-Tolylsulfinyl)phenyl]pentan-2-ol (4c). 4c was isolated diastereomerically pure by flash-column chromatography (AcOEt−hexane 1:1) of the crude mixture **4c** + **5c**. Yield 90% (method B), gummy; $[\alpha]^{20}_D$ −54.8 (*c* 0.7, $CHCl_3$); IR (film) 3019, 1083 cm^{-1}; ^{1}H NMR δ 7.77−7.74 (m, 1H), 7.45−7.20 (m, 7H), 3.66 (m, 1H), 2.92 (dd, J = 14.2 and 4.9 Hz, 1H), 2.86 (dd, J = 14.2 and 7.9 Hz, 1H), 2.59 (br s, OH), 2.34 (s, 3H), 1.51−1.24 (m, 4H), 0.86 (t, J = 6.8 Hz, 3H); ^{13}C NMR δ 143.4, 141.5, 141.0, 137.7, 131.1, 131.0, 129.9, 127.5, 125.9, 125.7, 71.2, 39.5, 39.1, 21.3, 18.8, 13.9; MS (EI) *m/z* 303 [M + 1]$^+$; HRMS [M + 1]$^+$ calcd for $C_{18}H_{23}O_2S$ 303.1419, found 303.1413.

[2*R*,(S)*S*]-1-[2-(*p*-Tolylsulfinyl)phenyl]pentan-2-ol (5c). 5c was isolated diastereomerically pure by flash-column chromatography (AcOEt−hexane 1:1) of the crude mixture **4c** + **5c**. Yield 61% (method C), gummy; $[\alpha]^{20}_D$ −96.4 (*c* 2.2, $CHCl_3$); ^{1}H NMR δ 7.80−7.76 (m, 1H), 7.46−7.22 (m, 7H), 3.79 (m, 1H), 2.84 (m, 2H), 2.63 (br s, OH), 2.36 (s, 3H), 1.58−1.25 (m, 4H), 0.93 (t, J = 4.8 Hz, 3H); ^{13}C NMR δ 143.2, 141.3, 141.1, 138.9, 131.5, 129.8, 127.3, 126.9, 125.3, 72.1, 40.0, 39.5, 21.2, 18.7, 13.9.

[2*R*,(S)*S*]-3-Methyl-1-[2-(*p*-tolylsulfinyl)phenyl]butan-2-ol (4d). 4d was isolated diastereomerically pure by flash-column chromatography (AcOEt−hexane 1:1) of the crude mixture **4d** + **5d**. Yield 91% (method B), gummy; $[\alpha]^{20}_D$ −33.6 (*c* 0.6, $CHCl_3$); IR (film) 3390, 1086, 839 cm^{-1}; ^{1}H NMR δ 7.72−7.66 (m, 1H), 7.46−7.22 (m, 7H), 3.40 (m, 1H), 2.89 (m, 2H), 2.35 (s, 3H), 1.71 (dsp, J = 6.8 and 2.0 Hz, 1H), 0.93 (dd, J = 6.8 and 1.6 Hz, 6H); ^{13}C NMR δ 143.6, 141.6, 140.8, 138.5, 131.1, 130.9, 129.9, 127.4, 126.0, 125.7, 76.5, 36.4, 33.6, 21.3 (2C), 18.8, 17.1; MS (EI) *m/z* 303 [M + 1]$^+$; HRMS [M + 1]$^+$ calcd for $C_{18}H_{23}O_2S$ 303.1419, found 303.1416.

[2*S*,(S)*S*]-3-Methyl-1-[2-(*p*-tolylsulfinyl)phenyl]butan-2-ol (5d). 5d could not be isolated diastereomerically pure. It was characterized from a mixture of **4d** + **5d** obtained by flash-column chromatography (AcOEt−hexane 1:1); ^{1}H NMR (representative parameters) δ 3.58 (ddd, J = 10.1, 4.9 and 3.2 Hz, 1H), 2.85 (dd, J = 13.7 and 10.1 Hz, 1H), 2.71 (dd, J = 13.7 and 3.2 Hz, 1H); ^{13}C NMR (representative parameters) δ 142.9, 141.3, 141.0, 139.9, 131.8, 130.0, 128.4, 127.1, 126.1, 125.1, 77,2, 36.0, 34.3, 18.5, 17.3.

C−S Bond Cleavage. General Procedure. Alkyllithium (0.85 mmol) was added to a solution of the corresponding hydroxysulfoxide (0.214 mmol) in THF (1.6 mL) under argon at −78 °C. The reaction was stirred for 10 min and then it was hydrolyzed with a saturated aqueous solution of NH_4Cl. The crude mixture was extracted with CH_2Cl_2 (3 × 5 mL) and dried ($MgSO_4$) and the solvent was evaporated.

(*S*)-1-Phenylpropan-2-ol (6a).[11a] **6a** was prepared by reaction of **4a** with *tert*-butyllithium. Purification was performed by flash-column chromatography (AcOEt−hexane 1:2). Yield 67%; colorless oil; $[\alpha]^{20}_D$ +36.0 (*c* 0.8, benzene) [lit.[11a] $[\alpha]_D$ +40.9 (*c* 0.5, benzene)]. Ee 99% (determined by integration of well-separated signals in the ^{1}H NMR spectra of the corresponding Mosher derivative). ^{1}H NMR values are in agreement with the reported values.

(*R*)-1,2-Diphenylethanol (6b).[11b] **6b** was prepared by reaction of **4b** with *n*-butyllithium. Purification was performed by flash-column chromatography (AcOEt−hexane 1:2). Yield 60%; colorless oil; $[\alpha]^{20}_D$ −43.5 (*c* 1.4, *i*-PrOH) [lit.[11b] $[\alpha]_D$ −42.0 (*c* 1.86, EtOH)]. Ee 99% (determined by integration of well-separated signals in the ^{1}H NMR spectra of the corresponding Mosher derivative). ^{1}H NMR values are in agreement with the reported values.

(*S*)-1-Phenylpentan-2-ol (6c).[11c] **6c** was prepared by reaction of **4c** with *tert*-butyllithium. Purification was performed by flash-column chromatography (AcOEt−hexane 1:2). Yield 54%; colorless oil; $[\alpha]^{20}_D$ +4.2 (*c* 1.8, EtOH) [lit.[11c] $[\alpha]_D$ +4.2 (*c* 0.57, EtOH)]. Ee 99% (determined by integration of well-separated signals in the ^{1}H NMR spectra of the corresponding Mosher derivative). ^{1}H NMR values are in agreement with the reported values.

(*R*)-3-Methyl-1-phenylbutan-2-ol (6d).[11d] **6d** was prepared by reaction of **4d** with *n*-butyllithium. Purification was performed by flash-column chromatography (AcOEt−hexane 1:2). Yield 70%; colorless oil; $[\alpha]^{20}_D$ +43.7 (*c* 1.5, MeOH). Ee 99% (determined by integration of well-separated signals in the ^{1}H NMR spectra of the corresponding Mosher derivative) [lit.[11d] $[\alpha]_D$ +4.6 (*c* 1.42, MeOH, 11% ee)]. ^{1}H NMR values are in agreement with the reported values.

[2*S*,3*R*,(S)*S*]-3-[2-(*p*-Tolylsulfinyl)phenyl)]butan-2-ol (7a). 7a was isolated diastereomerically pure by flash-column chromatography (AcOEt−hexane 1:2) of the crude mixture. Yield 70% (method B), 29% (method A), colorless oil; $[\alpha]^{20}_D$ −69.6 (*c* 5.1, $CHCl_3$); ^{1}H NMR δ 7.88−7.85 (m, 1H), 7.46−7.36 (AA′BB′ system, 4H), 7.25−7.21 (m, 3H), 3.90 (m, 1H), 3.21 (m, 1H), 2.35 (s, 3H), 1.95 (br s, 1H, OH), 1.23 (d, J = 5.9 Hz, 3H), 0.95 (d, 3H); ^{13}C NMR δ 142.9, 142.8, 141.9, 141.8, 131.2, 129.9, 127.5, 127.1, 126.0, 124.6, 72.2, 41.9, 21.6, 21.4, 16.4; MS (MALDI) *m/z* 271 [M + 1 − H_2O]; HRMS [M + 1]$^+$ calcd for $C_{17}H_{21}O_2S$ 289.1262, found 289.1265.

[2*R*,3*R*,(S)*S*]-3-[2-(*p*-Tolylsulfinyl)phenyl)]butan-2-ol (8a). 8a was isolated diastereomerically pure by flash-column chromatography (AcOEt−hexane 1:2) of the crude mixture **7a** + **8a**. Yield 44% (method A), colorless oil; $[\alpha]^{20}_D$ −99.9 (*c* 1.76, $CHCl_3$); ^{1}H NMR δ 8.01 (dd, J = 6.1 and 3.2 Hz, 1H), 7.51−7.42 (AA′BB′ system, 4H), 7.31−7.25 (m, 3H), 3.93 (dq, J = 6.9 and 6.5 Hz, 1H), 3.18 (dq, J = 6.9 and 5.7 Hz, 1H), 2.38 (s, 3H), 2.10 (br s, 1H, OH), 1.14 (d, J = 6.3 Hz, 3H), 1.04 (d, J = 6.5 Hz, 3H); ^{13}C NMR δ 143.8, 142.3, 141.8, 141.7, 131.2, 129.9, 127.6, 127.3, 126.1, 124.5, 72.0, 42.0, 21.3, 21.1, 17.4; MS (MALDI) *m/z* 271 [M + 1 − H_2O]; HRMS [M + 1] calcd for $C_{17}H_{21}O_2S$ 289.1262, found 289.1261.

[2*S*,3*S*,(S)*S*]-3-[2-(*p*-Tolylsulfinyl)phenyl]butan-2-ol (9a). 9a was isolated diastereomerically pure by flash-column chromatography (AcOEt−hexane 1:3) of the crude mixture **9a** + **10a**. Yield 52% (method B), colorless oil; $[\alpha]^{20}_D$ −62.5 (*c* 2.12, $CHCl_3$); ^{1}H NMR δ 7.82 (dd, J = 7.7 and 1.6 Hz, 1H), 7.49−7.37 (AA′BB′ system, 4H), 7.33 (dd, J = 7.7 and 1.6 Hz, 1H), 7.22 (m, 2H), 3.71 (dq, J = 6.5 and 5.7 Hz, 1H), 3.34 (dq, J = 6.9 and 5.7 Hz, 1H), 2.59 (br s, 1H, OH), 2.35 (s, 3H), 1.14 (d, J = 6.9 Hz, 3H), 0.84 (d, J = 6.5 Hz, 3H); ^{13}C NMR δ 143.9, 142.5, 141.6, 141.4, 131.5, 129.9, 128.5, 127.5, 127.2, 126.9, 126.0, 70.8, 40.5, 21.3, 19.9, 16.7; MS (MALDI) *m/z* 271 [M + 1 − H_2O]; HRMS [M + 1]$^+$ calcd for $C_{17}H_{21}O_2S$ 289.1262, found 289.1263.

(2*R*,3*S*,(S)*S*)-3-[2-(*p*-Tolylsulfinyl)phenyl)]butan-2-ol (10a). 10a was isolated diastereomerically pure by flash-column chromatography (AcOEt−hexane 1:3) of the crude mixture **9a** + **10a**. Yield 42% (method B), colorless oil; $[\alpha]^{20}_D$

−79.3 (*c* 2.25, $CHCl_3$); IR (film) 3405, 1083, 1009 cm^{-1}; ^1H NMR δ 7.76 (dd, *J* = 7.7 and 1.2 Hz, 1H), 7.52−7.41 (AA′BB′ system, 4H), 7.38−7.22 (m, 3H), 3.72 (dq, *J* = 8.5 and 6.1 Hz, 1H), 3.37 (dq, *J* = 8.5 and 6.9 Hz, 1H), 2.40 (br s, 1H, OH), 2.36 (s, 3H), 1.22 (d, *J* = 6.1 Hz, 3H), 1.04 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR δ 145.4, 143.2, 141.8, 140.9, 132.2, 129.7, 127.7, 127.1, 125.2, 72.5, 42.0, 21.7, 21.3.

(*S*)-3-Phenyl-2-butanol (11). The sulfoxide **7a** (0.079 mmol) was dissolved in a minimal amount of absolute EtOH and an excess of activated Raney nickel was added. The reaction was stirred for 1 h at room temperature, then filtered through a Celite pad, and the residue was purified by chromatography (AcOEt−hexane 1:2) to give a colorless oil. Yield 71%; $[\alpha]_D$ +19.1 (*c* 3.0, EtOH) [lit.[14] $[\alpha]_D$ +16.2 (*c* 3.6, EtOH), 81% ee]. ^1H NMR values are in agreement with the reported values.[15]

Sulfinyl Group Oxidation. General Procedure. A solution of the corresponding hydroxysulfoxides in $CDCl_3$ was added to a NMR tube containing an excess of previously dried ($MgSO_4$) MCPBA solution in the same solvent. The NMR signals were obtained from the crude mixtures.

(2*R*,3*S*)-2-[2-(*p*-Tolylsulfonyl)phenyl)]-3-butanol (12). **12** was obtained by MCPBA oxidation from hydroxysulfoxide **7a**. ^1H NMR δ 8.10−7.31 (m, 8H), 3.71 (m, 1H), 3.51 (m, 1H), 2.40 (s, 3H), 1.16 (d, *J* = 6.1 Hz, 3H), 6.9 (d, *J* = 6.9 Hz, 3H).

(2*S*,3*R*)-2-[2-(*p*-Tolylsulfonyl)phenyl)]-3-butanol (*ent*-12). *ent*-**12** was obtained by MCPBA oxidation from hydroxysulfoxide **10a**. ^1H NMR δ 8.10−7.31 (m, 8H), 3.71 (m, 1H), 3.51 (m, 1H), 2.40 (s, 3H), 1.16 (d, *J* = 6.1 Hz, 3H), 6.9 (d, *J* = 6.9 Hz, 3H).

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Supporting Information Available: ^1H and ^{13}C NMR spectra of compounds **4a**−**d**, **5a**−**d**, **6a**−**d**, **7a**−**10a**, and **11** (^1H NMR). This material is available free of charge via the Internet at http://pubs.acs.org.

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