Catalytic Asymmetric Oxidation of Aryl Sulfides with a Ti/H_2O/(*R,R*)-Diphenylethane-1,2-diol Complex: a Versatile and Highly Enantioselective Oxidation Protocol

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A new catalytic procedure for the asymmetric oxidation of aryl alkyl and aryl benzyl sulfides to optically active sulfoxides by hydroperoxides is described. This oxidation of sulfides is mediated by a chiral Ti complex formed in situ by reacting Ti(*i*-PrO)$_4$, (*R,R*)-diphenylethane-1,2-diol (**1**), and water. The conditions of the reaction (stoichiometric composition of the catalyst, temperature, and the presence of additives and solvent) have been determined in order to reach the highest enantioselectivity and avoid the intervention of a kinetic resolution process. The oxidation protocol described herein is quite versatile as the values of chemical yields (60−73%) and of enantioselectivity (ee 70−80%) achieved for aryl alkyl sulfides are almost independent of the nature of the aryl substituent and of the size of the alkyl group. Notably, aryl benzyl sulfides, which are poor substrates for the Ti/DET catalyzed oxidations, afforded very high ee's (92−99%) with this oxidation system.

Introduction

In the past few years, the synthesis of optically active sulfoxides through asymmetric oxidation of prochiral sulfides[1] has constituted a very active research area, owing to the relevance of enantiopure sulfoxides as chiral auxiliaries,[2] synthetic intermediates, and bioactive compounds.[3] In the most widely studied procedure, the oxidation is performed by achiral hydroperoxides in the presence of stoichiometric amounts of chiral Ti(IV) complexes[4] and, very recently, the use of chiral hydroperoxides with achiral Ti species has been reported as well.[5] Several appealing asymmetric catalytic processes also have been described in the literature,[6] all showing as a common feature the formation in situ of a catalytic precursor by reaction of Ti(*i*-PrO)$_4$ with chiral dihydroxyl ligands such as (*R,R*)-diethyl tartrate (DET),[6a,b] 2,2′-dihydroxy-1,1′-binaphthyl,[6c] trialkanolamines,[6d] and simple 1,2-diols.[6e,f] These catalytic procedures, however, present some limitations; in fact, the Kagan method[6a,b] requires 0.1 equiv of Ti(*i*-PrO)$_4$ and 0.4 equiv of DET with respect to the sulfide and hence cannot be considered as truly catalytic. In addition, in most of the catalytic procedures reported, the high ee's obtained are mainly due to a kinetic resolution process[7] (i.e., the two enantiomers of the sulfoxide are oxidized to sulfone by the chiral reagent at different rates) with detriment to the chemical yields. We preliminarily described[6e] a different oxidation system based on a catalyst formed in situ by reacting Ti(*i*-PrO)$_4$, enantiopure 1,2-diphenylethane-1,2-diol (**1**), and water (Scheme 1), aimed at inducing enantioselectivity *only* in the formation of the sulfoxides and making negligible the kinetic resolution. In this paper we will discuss in detail the efficiency of our oxidation method, by analyzing the dependence of ee and chemical yield on the reaction conditions, on the composition of the catalyst, and on the structure of the substrate.

Results and Discussion

As briefly discussed in the Introduction, the main target of the present investigation was to set up a method for the asymmetric catalytic oxidation of sulfides devoid of kinetic resolution, in order to keep both the enantioselectivity and the chemical yield of the overall process

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(1) Kagan, H. B. Asymmetric Oxidation of Sulfides. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993; pp 203−226.

(2) Carreño, M. C. *Chem. Rev.* **1995**, *95*, 1717. Solladié, G. *Synthesis* **1981**, 185. Andersen, K. K. In *The Chemistry of Sulfones and Sulfoxides*; Patai, S., Rappoport, Z., Stirling, C. J. M., Eds.; John Wiley & Sons, Ltd.: Chichester, England, 1988; Chapter 3, pp 53−94. Posner, G. H. In *The Chemistry of Sulfones and Sulfoxides*; Patai, S., Rappoport, Z., Stirling, C. J. M., Eds.; John Wiley & Sons, Ltd.: Chichester, England, 1988; Chapter 16, pp 823−849.

(3) (a) **RP 73163**: Pitchen, P. *Chem. Ind.* **1994**, Aug 15, 636. (b) **Pantoprazole**: Tanaka, M.; Yamazaki, H.; Hakasui, H.; Nakamichi, N.; Sekino, H. *Chirality* **1997**, *9*, 17. (c) **Omeprazole**: von Unge, S.; Langer, V.; Sjölin, L. *Tetrahedron: Asymmetry* **1997**, *8*, 1967. (d) **Sulforafane**: Holland, H. L.; Brown, F. M.; Larsen, B. G. *Tetrahedron: Asymmetry* **1994**, *5*, 1129. (e) **Ustiloxine**: Hutton, C. A.; White, J. M. *Tetrahedron Lett.* **1997**, *38*, 1643. (f) **OPC-29030**: Morita, S.; Matsubara, J.; Otsubo, K.; Kitano, K.; Ohtani, T.; Kawano, Y.; Uchida, M. *Tetrahedron: Asymmetry* **1997**, *8*, 3707. (g) **Methionine Sulfoxide**: Holland, H. L.; Brown, F. M. *Tetrahedron: Asymmetry* **1998**, *9*, 535.

(4) (a) Pitchen, P.; Duñach, E.; Deshmukh, M. N.; Kagan, H. B. *J. Am. Chem. Soc.* **1984**, *106*, 8188. (b) Zhao, S.; Samuel, O.; Kagan, H. B. *Tetrahedron* **1987**, *43*, 5135. (c) Kagan, H. B.; Rebiere, F. *Synlett* **1990**, 643. (d) Brunel, J.-M.; Diter, P.; Duetsch, M.; Kagan, H. B. *J. Org. Chem.* **1995**, *60*, 8086. (e) Di Furia, F.; Modena, G.; Seraglia, G. *Synthesis* **1984**, 325. (f) Yamamoto, K.; Ando, H.; Shuetake, T.; Chikamatsu, H. *J. Chem. Soc., Chem. Commun.* **1989**, 754.

(5) (a) Adam, W.; Korb, M. N.; Roschmann, K. J.; Saha-Möller, C. *J. Org. Chem.* **1998**, *63*, 3423. (b) Hamann, H.-J.; Höft, E.; Mostowicz, D.; Mishnev, A.; Urbanczyk-Lipkowska, Z.; Chmielewski, M. *Tetrahedron* **1997**, *53*, 185.

(6) (a) Brunel, J.-M.; Kagan, H. B. *Synlett* **1996**, 404. (b) Brunel, J.-M.; Kagan, H. B. *Bull. Soc. Chim. Fr.* **1996**, *133*, 1109. (c) Komatsu, N.; Hashizume, M.; Sugita, T.; Uemura, S. *J. Org. Chem.* **1993**, *58*, 4529. (d) Di Furia, F.; Licini, G.; Modena, G.; Motterle, R.; Nugent, W. A. *J. Org. Chem.* **1996**, *61*, 5175. (e) Superchi, S.; Rosini, C. *Tetrahedron: Asymmetry* **1997**, *8*, 349. (f) Yamanoi, Y.; Imamoto, T. *J. Org. Chem.* **1997**, *62*, 8560.

(7) (a) Komatsu, N.; Hashizume, M.; Sugita, T.; Uemura, S. *J. Org. Chem.* **1993**, *58*, 7624. (b) Lattanzi, A.; Bonadies, F.; Senatore, A.; Soriente, A.; Scettri, A. *Tetrahedron: Asymmetry* **1997**, *8*, 2473.

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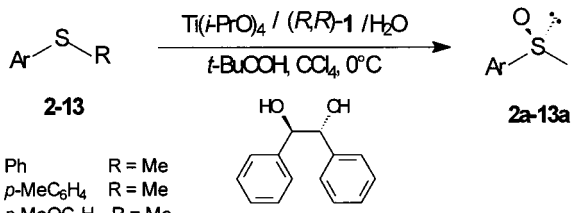
Scheme 1



2 Ar = Ph R = Me
3 Ar = *p*-MeC_6H_4 R = Me
4 Ar = *p*-$MeOC_6H_4$ R = Me
5 Ar = *p*-BrC_6H_4 R = Me
6 Ar = *p*-$NO_2C_6H_4$ R = Me
7 Ar = 2-Naphthyl R = Me
8 Ar = Ph R = Et
9 Ar = Ph R = *n*-Bu
10 Ar = Ph R = *i*-Pr
11 Ar = Ph R = $PhCH_2$
12 Ar = *p*-MeC_6H_4 R = $PhCH_2$
13 Ar = *p*-$MeOC_6H_4$ R = $PhCH_2$

at high levels. In our preliminary study[6e] we optimized the reaction conditions (temperature, reaction time, and amount of catalyst and oxidant). Moreover, we observed that extending the reaction time for more than 2 h resulted in an increase in the amount of sulfone without raising either the yield or the ee of the sulfoxide. This was due to an inactivation process of the catalyst determined by decomposition of the diol[6e] and/or complexation of the titanium center by the sulfoxide.[4a,5a] The complexation at titanium can also promote the further oxidation of sulfoxide to sulfone.[8] We then found that the best compromise to limit the sulfone formation and to have satisfactory conversion and good ee's was achieved using the reagent ratio sulfide:(*R*,*R*)-**1**:Ti:H_2O = 1:0.1:0.05:1.0 with 2 equiv of TBHP 70% in water as oxidant and performing the reaction at 0 °C in CCl_4 under N_2 atmosphere. These optimized reaction conditions, hereafter named as *standard*, were then used as the basis for the following investigations.

The effect of the composition of the catalytic precursor and the presence of additives was then studied in the oxidation of *p*-tolyl methyl sulfide (**3**) (Table 1). The use of anhydrous TBHP (entry 2) led to a similar chemical yield and to a slightly lower ee with respect to the levels obtained with the standard conditions (entry 1). Changing the Ti:diol ratio from 1:2 (standard condition) to 1:1 reduced both the chemical yield and the enantioselectivity, which dropped to 18% ee (entry 3). The addition of molecular sieves and 2-propanol as additives, which were beneficial under the Kagan conditions,[6a,b] proved to be detrimental in our hands, because both in CCl_4 and in CH_2Cl_2 we obtained a reduced yield and a lower enantiomeric excess of sulfoxide, with significant formation of sulfone (entries 4 and 5).

In Table 2, the results of a systematic change of the solvent are reported: the highest ee's were obtained in CCl_4 (entry 4) and toluene (entry 5), while CH_2Cl_2 (entry 3) and ethereal solvents (entries 1, 2) reduced both the chemical yield and the ee of the sulfoxide. In hexane, a white solid precipitated when water was added to the reaction mixture, while all other solvents tested gave rise to homogeneous mixtures. The chemical yields and the enantioselectivities (entry 6) were, however, comparable with those in CCl_4. More detailed investigations on the nature and activity of both the solution and the solid phase are now in progress.

We then investigated if a kinetic resolution process was present under our reaction conditions: to this end, racemic *p*-tolyl methyl sulfoxide (**3a**) was reacted under the standard conditions using (*R*,*R*)-**1** as chiral ligand, and a time profile of the amount of sulfoxide **3a** and of sulfone, as well as the ee of the sulfoxide was plotted (Figure 1). We can observe from the plot that the kinetic resolution process leads to significant levels of sulfoxide ee (30%) only for very long reaction times and at high levels of conversion. This means that the efficiency of the kinetic resolution is low (a selectivity factor[9] S = 1.5−2 can be calculated) and that, in the short reaction times employed under our standard conditions (≈2 h), its effect is negligible.

Once the best reaction conditions were set up in terms of both chemical yield and enantioselectivity, it was important to evaluate the scope and limitations of this method. To this end, several aryl alkyl and benzyl sulfides (compounds **2**−**13**, Table 3), differing in the nature of the Ar and R groups, were prepared using standard procedures[10] and then submitted to the action of our oxidation system, obtaining the corresponding sulfoxides **2a**−**13a**. The results of such reactions are collected in Table 3.

Compounds **2a**−**12a** have been already reported in optically active form,[4a,6b,11] so the absolute configuration of the samples in our hands has been assigned on the basis of their $[\alpha]_D$ values (Table 3, entries 1−11). To the best of our knowledge, the absolute configuration of *p*-anisyl benzyl sulfoxide (**13a**) (entry 12) is unknown, so it was necessary to compare its CD spectrum (350−200 nm range) with that of the known (*R*)-(+)-*p*-tolyl benzyl sulfoxide (**11a**).[12] The CD spectrum of our sample of (−)-**13a** shows a negative Cotton effect at 252 nm followed by a positive Cotton effect at 230 nm, while the CD spectrum of (*R*)-(+)-**11a** shows[13] bands of opposite sign at the same frequencies. This indicates that the levorotatory sample in our hands has the *S* absolute configuration. The ee's of our samples have been determined by HPLC analysis upon the chiral stationary phases Chiralcel OB and OJ, using hexane/*i*-PrOH mixtures as mobile phases. The racemic sulfoxides necessary to test the products' separation were prepared by standard procedures.[14]

Good chemical yields of isolated products, in the 60−80% range, were obtained for all cases, with these being almost independent of the structure of the sulfide. Furthermore, the use of (*R*,*R*)-**1** as ligand always induced the formation of sulfoxides having the *S* absolute configuration, thus indicating that the same mechanism seems to be operative independently of the structure of the substrate. This behavior parallels what is observed

(8) Some exploratory runs showed that diol **1** slowly decomposes in the presence of Ti(*i*-PrO)$_4$, while a partial decomposition to benzaldehyde results after further addition of TBHP. Moreover, we observed that TBHP alone does not oxidize the sulfoxide while it promotes a slow oxidation of the sulfide.

(9) Kagan, H. B.; Fiaud, J. C. *Top. Stereochem.* **1988**, *18*, 249.

(10) Ipatieff, V. N.; Pines, H.; Friedmann, B. S. *J. Am. Chem. Soc.* **1938**, *60*, 2731.

(11) (a) Sakuraba, H.; Natori, K.; Tanaka, Y. *J. Org. Chem.* **1991**, *56*, 4124. (b) Sugimoto, T.; Kokubo, T.; Miyazaki, J.; Tanimoto, S.; Okano, M. *J. Chem. Soc., Chem. Commun.* **1979**, 402.

(12) The assignment of absolute configuration of sulfoxides via analysis of CD spectra has already been reported: Sagae, T.; Ogawa, S.; Furukawa, N. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 3179.

(13) Saeva, F. D.; Rayner, D. R.; Mislow, K. *J. Am. Chem. Soc.* **1968**, *90*, 4176.

(14) Leonard, N. J.; Johnson, C. R. *J. Org. Chem.* **1962**, *27*, 282.

Table 1. Enantioselective Oxidation of *p*-Tolyl Methyl Sulfide: Effect of Catalyst Composition and Additives

entry	conditions:[a] sulfide/(*R*,*R*)-**1**/Ti	solvent	additive (equiv)	oxidant (equiv)	sulfoxide (%)[b]	ee[c] (%) (ac)[d]
1	1/0.1/0.05	CCl_4	H_2O (1.0)	TBHP (2.0)[e]	62 (8)	80 (*S*)
2	1/0.1/0.05	CCl_4	H_2O (1.0)	TBHP (2.0)[f]	63 (7)	60 (*S*)
3	1/0.05/0.05	CCl_4	H_2O (1.0)	TBHP (2.0)[e]	50 (12)	18 (*S*)
4	1/0.1/0.05	CH_2Cl_2	*i*-PrOH (0.2) + 4 Å MS	CHP (2.0)[g]	45 (32)	20 (*S*)
5	1/0.1/0.05	CCl_4	*i*-PrOH(0.2) + 4 Å MS	CHP (2.0)[g]	30 (26)	24 (*S*)

[a] Under N_2 atmosphere, reaction time 2 h. [b] Isolated yields, in parentheses sulfone (%). [c] Determined by HPLC on a Daicel Chiralcel OB column. [d] Absolute configuration (ac) determined by comparison of $[\alpha]_D$ with literature values; see ref 4a. [e] TBHP 70% in water. [f] TBHP 5−6 M in decane. [g] CHP 80% in cumylic alcohol.

Table 2. Enantioselective Oxidation of *p*-Tolyl Methyl Sulfide: Effect of Solvent[a]

entry	solvent	sulfoxide (%)[b]	ee[c] (%) (ac)[d]
1	THF	56 (5)	16 (*S*)
2	Et_2O	50 (18)	36 (*S*)
3	CH_2Cl_2	74 (4)	54 (*S*)
4	CCl_4	62 (8)	80 (*S*)
5	toluene	70 (9)	70 (*S*)
6	hexane	55 (3)	80 (*S*)

[a] Conditions: sulfide/(*R*,*R*)-**1**/Ti(*i*-PrO)$_4$/H_2O = 1.0/0.1/0.05/1.0 at 0 °C under N_2 atmosphere, reaction time 2 h, 2 equiv of 70% TBHP in water as oxidant. [b] Isolated yields, in parentheses sulfone (%). [c] Determined by HPLC on a Daicel Chiralcel OB column. [d] Absolute configuration (ac) determined by comparison of $[\alpha]_D$ with literature values; see ref 4a.

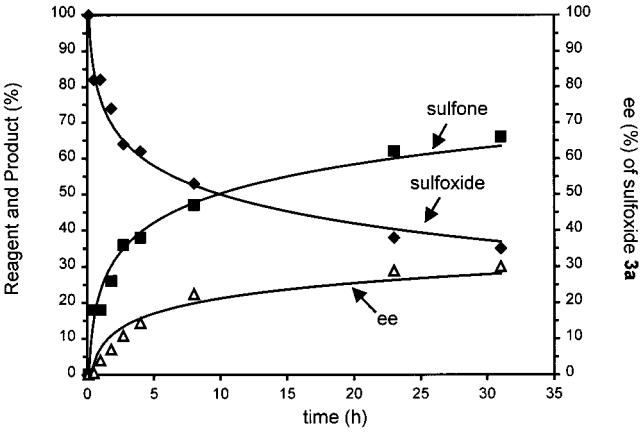


Figure 1. Time profile of the oxidation of racemic sulfoxide **3a** under the *standard* conditions. (Study of the intervention of kinetic resolution.)

in sulfoxidation with Ti/DET complexes, where (*R*,*R*)-DET, having absolute configuration opposite to that of (*R*,*R*)-**1**, induces the formation of *R* sulfoxides. Surprisingly, the similar diol (3*S*,4*S*)-2,2,5,5-tetramethyl-3,4-hexanediol induces the formation of *S* sulfoxides.[6f] Remarkably, only negligible amounts of sulfone were formed in all the entries, confirming that the enantioselectivity obtained was completely induced during the sulfide oxidation process and not due to a concomitant kinetic resolution. By changing the aromatic substituents in aryl methyl sulfides, we showed that our oxidation system is almost unaffected by the nature of the aryl moiety. Sulfides with electron-donating groups (entries 2−4) on the phenyl ring, as well as those with a larger naphthyl ring, were oxidized affording ee's in the 70−80% range. The lower ee obtained in the case of *p*-NO_2-substituted sulfide **6** (entry 5) could be attributed either to the strong electron-withdrawing power or, even more reasonably, to the coordinating capability of the nitro group, which can effect a change of the reaction mechanism and then a reduction of the enantioselectivity. Recently it has been shown that the presence of nitro groups on the ligand can heavily affect the stereochemical outcome of a Ti-catalyzed asymmetric sulfoxidation.[15] It is noteworthy that our system is almost unaffected also by the size of the alkyl R group on the sulfur. In fact, high ee's have been obtained with both ethyl (ee 70%) and *n*-butyl (ee 80%) substituted sulfides (entries 7, 8), the latter being *the highest ee obtained so far in the Ti-catalyzed enantioselective oxidation of aryl butyl sulfides*. Only the presence of a branched and sterically demanding alkyl substituent, like the isopropyl moiety in **10** (entry 9), led to a significant drop of the enantioselectivity.

In summary, the present oxidation protocol looks quite versatile because the chemical and stereochemical outcomes are only slightly dependent on the nature of the Ar and R groups of the sulfides. On the contrary, the diethyltartrate[6a,b] and binaphthol-based[6c] catalysts are effective only on sulfides having small R groups, while the trialkanolamine reagent[6d] is sensitive to the nature of the Ar substituents. Finally, it is important to point out that aryl benzyl sulfides **11**−**13**, oxidized with the Ti/DET complex in very low ee,[4a] were, on the contrary, *transformed to the corresponding sulfoxides with almost complete stereoselectivity* (ee 92−99%) by the oxidation system described herein. Taking into account the presence of several benzene rings, both on the substrate and on the catalyst, it is tempting to ascribe to $\pi-\pi$ interactions[16] the main cause of such a selectivity.[17] In addition, the high enantioselectivity that is achievable for aryl benzyl sulfides is very promising with regard to the synthesis of chiral bioactive sulfoxides.[3] As a matter of fact, several of these sulfoxides have an aryl(heteroaryl) benzyl structure, and their preparation through the enantioselective oxidation of the corresponding sulfides could be particularly appealing.

Conclusions

We have herein described the catalytic asymmetric oxidation of aryl sulfides with TBHP mediated by 0.05 equiv of a chiral Ti complex formed in situ by reacting Ti(*i*-PrO)$_4$, (*R*,*R*)-**1**, and water. In this way, optically active sulfoxides are obtained in good yields (60−75%) and good to high ee's (up to 99%).

It is important to point out that even compounds such as *p*-substituted phenyl benzyl sulfides, which afford low

(15) Reetz, M. T.; Merk, C.; Naberfeld, G.; Rudolph, J.; Griebenow, N.; Goddard, R. *Tetrahedron Lett.* **1997**, *38*, 5273.

(16) The importance of $\pi-\pi$ interaction in asymmetric synthesis has been recently pointed out: Jones, G. B.; Chapman, B. J. *Synthesis* **1995**, 475. For a recent discussion about the arene−arene interactions see: Hunter, C. A. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1585. Hunter, C. A. *Chem. Soc. Rev.* **1994**, 101. Cozzi, F.; Siegel, J. S. *Pure Appl. Chem.* **1995**, *67*, 1995.

(17) It is interesting to point out that also in Ti-trialkanolamine catalyzed oxidations, (see ref 6d) the highest enantioselectivity (ee 84%) is achieved when phenyl benzyl sulfide is oxidized with the (*R*,*R*,*R*)-tris(2-hydroxy-2-phenylethyl)amine complex, i.e., with a ligand bearing phenyl groups.

Table 3. Enantioselective Oxidation of Sulfides 2-13 (ArSR)[a]

entry	sulfide	Ar	R	sulfoxide (%)[b]	ee[c] (%) (ac)[d]
1	**2**	Ph	Me	63	80 (*S*)
2	**3**	*p*-MeC_6H_4	Me	62	80 (*S*)
3	**4**	*p*-$MeOC_6H_4$	Me	55	69 (*S*)
4	**5**	*p*-BrC_6H_4	Me	58	67 (*S*)
5	**6**	*p*-$NO_2C_6H_4$	Me	74	44 (*S*)
6	**7**	2-naphthyl	Me	65	73 (*S*)
7	**8**	Ph	Et	71	70 (*S*)
8	**9**	Ph	*n*-Bu	69	80 (*S*)
9	**10**	Ph	*i*-Pr	60	22 (*S*)
10	**11**	Ph	$PhCH_2$	73	>99[e] (*S*)
11	**12**	*p*-MeC_6H_4	$PhCH_2$	65	98[e] (*S*)
12	**13**	*p*-$MeOC_6H_4$	$PhCH_2$	60	92[e] (*S*)

[a] Conditions: sulfide/(*R*,*R*)-**1**/Ti(*i*-PrO)$_4$/H_2O = 1.0/0.1/0.05/1.0 in CCl_4 at 0 °C under N_2 atmosphere, reaction time 2 h, 2 equiv of 70% TBHP in water as oxidant. [b] Isolated yields, amount of sulfone < 10%. [c] Determined by HPLC on a Daicel Chiralcel OB column. [d] Absolute configuration (ac) determined by comparison of $[\alpha]_D$ with literature values; see refs 4a,d, 11. [e] Determined by HPLC on a Daicel Chiralcel OJ column.

ee's in both chemical Ti-catalyzed[4a] and enzymatic[18] sulfoxidation procedures, are oxidized with high or complete stereoselectivity. This aspect has important practical (synthesis of bioactive sulfoxides having an aryl benzyl structure) and theoretical (understanding of the interaction which determines the stereoselectivity) consequences. Furthermore, the chiral inducer (*R*,*R*)-**1** is easily available in both enantiomeric forms via Sharpless asymmetric dihydroxylation[19] of (*E*)-stilbene. This means that the present approach can be further developed considering that many other different 1,2-diarylethane-1,2-diols can become easily available through dihydroxylation of the corresponding (*E*)-1,2-diarylethenes. This could allow the study of the effects of both the steric and electronic properties of the ligand on the chemical and stereochemical outcomes of the reaction. This could further improve the chemical yields and the ee and help to define the stereochemical aspects of the reaction mechanism. Studies in this direction are now in progress.

Experimental Section

General Procedures. Melting points are uncorrected. ^1H NMR (300 MHz) spectra were recorded in $CDCl_3$. Toluene, Et_2O, and THF were freshly distilled over sodium benzophenone ketyl under a nitrogen atmosphere prior to their use. CCl_4 and CH_2Cl_2 were distilled from CaH_2 and P_2O_5, respectively, and stored over activated 4 Å molecular sieves. Ti(*i*-PrO)$_4$ was distilled under a nitrogen atmosphere prior to use. Commercially available *tert*-butyl hydroperoxide (TBHP) (70% in water and 5−6.0 M in decane) and cumyl hydroperoxide (CHP) (80% in cumyl alcohol) were purchased (Aldrich) and used without further purification. Phenyl methyl sulfide (**2**), *p*-tolyl methyl sulfide (**3**) and phenyl benzyl sulfide (**11**) were used as purchased (Aldrich); *p*-nitrophenyl methyl sulfide (**6**) (Aldrich) was recrystallized from hexane prior to use. The other aryl alkyl sulfides were prepared from the corresponding thiols according to literature procedure.[10] Enantiomerically pure (*R*,*R*)-1,2-diphenylethane-1,2-diol (**1**) was prepared by asymmetric dihydroxylation[19] of (*E*)-stilbene. Racemic sulfoxides were prepared by oxidation of the corresponding sulfides with 0.5 M KIO_4 according to a literature procedure.[14] The identity of sulfones was established by ^1H NMR and GLC-MS when their amounts were sufficient for isolation; otherwise, traces of sulfone were directly detected by GLC−MS of the crude mixture. Analytical and preparative TLC were performed on Merck 60 F-254 silica gel plates (0.2 mm and 2.0 mm, respectively), and column chromatography was carried out with Merck 60 silica gel (80−230 mesh).

Standard Procedure for Catalytic Oxidation of Sulfides. To a suspension of (*R*,*R*)-**1** (34.3 mg, 0.16 mmol) in CCl_4 (5 mL) were added dropwise in sequence Ti(*i*-PrO)$_4$ (23.6 μL, 0.08 mmol) and H_2O (28.8 μL, 1.6 mmol). To the resulting homogeneous solution was added phenyl methyl sulfide (**2**) (189 μL, 1.61 mmol), and the mixture was stirred at room temperature for 15 min. The solution was then cooled at 0 °C, and TBHP (70% in water, 440 μL, 3.22 mmol) was added. The mixture was stirred at 0 °C for 2 h, then diluted with CH_2Cl_2, and dried over Na_2SO_4 for a few minutes. After filtration and evaporation of solvent, the residue was immediately purified by preparative TLC (Et_2O as eluent) or column chromatography (EtOAc) isolating the phenyl methyl sulfoxide (**2a**) in 63% yield and phenyl methyl sulfone in 8% yield. The spectral data of the sulfoxides **2a**−**12a** matched those reported.[4a,6b,11] The ee of sulfoxides **2a**−**10a** was determined by HPLC on a Daicel Chiralcel OB column (λ 254 nm; *n*-hexane:*i*-PrOH = 80:20; flow = 0.8 mL/min for **2a**, **3a**, **4a**; flow = 0.5 mL/min for **5a**, **7a**; flow = 1.0 mL/min for **6a**, **10a**; *n*-hexane:*i*-PrOH = 90:10; flow = 1.0 mL/min for **8a**, **9a**) and the ee of sulfoxides **11a**−**13a** on a Daicel Chiralcel OJ column (λ 254 nm; *n*-hexane:*i*-PrOH = 80:20; flow = 0.8 mL/min for **11a**; flow = 1.0 mL/min for **12a, 13a**). In all cases the *S* enantiomer eluted first.

(*S*)-(−)-*p*-Anisyl Benzyl Sulfoxide (13a). Oxidation of *p*-anisyl benzyl sulfide (**13**) by the standard procedure afforded, after purification, 148 mg of **13a** (60% yield) as a white solid: ee = 92%; mp 130−132 °C; ^1H NMR δ 3.85 (s, 3H), 3.98 (d, *J* = 12.4 Hz, 1H), 4.12 (d, *J* = 12.4 Hz, 1H), 6.96 (m, 4H), 7.30 (m, 5H); IR (KBr) 1035 (S=O) cm^{-1}; $[\alpha]_D$ = −47.1 (*c* = 1.03, acetone).

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(18) Holland, L. H. *Chem. Rev.* **1988**, *88*, 473.
(19) Kolb, H. C.; Van Nieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483.