The First Chiral Zirconium(IV) Catalyst for Highly Stereoselective Sulfoxidation

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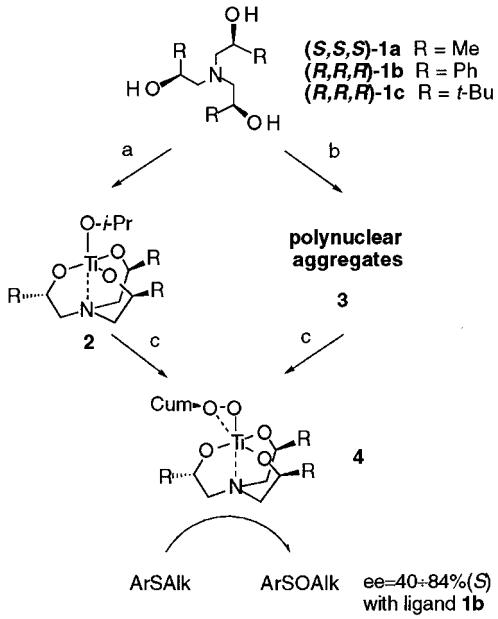
Catalytic enantioselective oxidations are among the most challenging transformations in asymmetric synthesis.[1] In particular, together with stereoselective osmium-catalyzed dihydroxylations[2] and salen−manganese-mediated epoxidation,[3] asymmetric oxidations catalyzed by chiral titanium(IV) alkoxides play a major role in this area.[4−8] Chiral titanium(IV) alkoxides have been found to mediate effectively some fundamental oxidative processes such as allylic alcohol epoxidation,[4] β-hydroxyamine *N*-oxidation,[5] sulfoxidation,[6,7] and Baeyer Villiger oxidation.[8] In contrast, analogous zirconium(IV) catalysts have been less extensively investigated. In the few example reported so far, they typically exhibit lower catalytic activity and poorer stereoselectivity compared with their titanium counterparts.[9] For example, in the epoxidation of (*E*)-α-phenylcinnamyl alcohol by *tert*-butyl hydroperoxide (TBHP), Zr(*i*-PrO)$_4$/(+)-diethyltartrate (DET) affords the corresponding (*R*,*R*)-epoxide in low yield and ee = 10%, while the Ti(IV) analogue produces the (*S*,*S*)-epoxide with ee > 95% in 75% yield.[9a,10] Higher stereoselections were obtained in the Zr(IV)/(+)-dicyclohexyltartramide-mediated epoxidation of homoallylic alcohols,[9b] which provides ee's up to 77% with yields ≤ 38%.

Scheme 1[a]



[a] Reagents and conditions: (a) Ti(*i*-PrO)$_4$ (1 equiv), CH_2ClCH_2Cl (DCE), 20 °C; (b) Ti(*i*-PrO)$_4$ (0.75 equiv), CH_2Cl_2, 20 °C, followed by solvent removal and hexane stripping; (c) $PhCMe_2OOH$ (CHP).

We recently reported that titanium complexes bearing C_3 symmetric trialkanolamine ligands **1a**−**c**[11,12] are effective catalysts for asymmetric sulfoxidation using alkyl hydroperoxides as the stoichiometric oxidant (Scheme 1).[7,13−15]

When the oxidation is performed with cumyl hydroperoxide (CHP) in the presence of catalysts **2b** or **3b**, high turnover numbers (TO) (1−2% catalyst loading) and enantiomeric excesses (ee's) in the range of 40−84% are obtained.[7]

We now report that a partially hydrolyzed zirconium catalyst bearing the same polydentate ligand **1b** can provide even higher levels of enantioselection with a larger number of alkyl aryl sulfides. Stereoselective sulfoxidations mediated by this new catalyst are characterized by (i) good catalytic performance (2% catalyst loading), (ii) ee's in the range 80−90%, resulting from the cooperativity of two oxidative stereoselective processes (vide infra), and (iii) the opposite enantioselection as compared with the corresponding titanium-catalyzed oxidations. Moreover, sulfinyl componds with poor steric differentiation between the two substituents at the sulfur atom (sterically balanced), such as benzyl, *tert*-butyl,

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(1) Ojima, I. *Catalytic Asymmetric Synthesis*; VCH Publisher: New York, 1993. Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; Wiley-Interscience: New York, 1994.
(2) Johnson, R. A.; Sharpless, K. B. In ref 1, Chapter 4.4, pp 103−158. Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483. Balavoine, G. G. A.; Manoury, E. *Appl. Organomet. Chem.* **1995**, *9*, 199.
(3) Jacobsen, E. N. In ref 1, Chapter 4.2, pp 159−202. Katsuki, T. *Coord. Chem. Rev.* **1995**, *140*, 189.
(4) Johnson, R. A.; Sharpless, K. B. In ref 1, Chapter 4.4, pp 227−272.
(5) Miyano, S.; Lu, L. D.-L.; Viti, S. M.; Sharpless, K. B. *J. Org. Chem.* **1983**, *48*, 3608.
(6) (a) Kagan, H. B. In ref 1, Chapter 4.3, pp 203−226, and references therein. (b) Mata, E. G. *Phosphorus, Sulfur Silicon* **1996**, *117*, 231, and references therein. (c) Brunel, J.-M.; Kagan, H. B. *Synlett* **1996**, 404. (d) Superchi, S.; Rosini, C. *Tetrahedron: Asymmetry* **1997**, *8*, 349. (e) Yamanoi, Y.; Imamoto, T. *J. Org. Chem.* **1997**, *62*, 8560. (f) Reetz, M. T.; Merk, C.; Naberfeld, G.; Rudolph, J.; Griebenow, N.; Goddard, R. *Tetrahedron Lett.* **1997**, *38*, 5273.
(7) Di Furia, F.; Licini, G.; Modena, G.; Motterle R.; Nugent, W. A. *J. Org. Chem.* **1996**, *61*, 5175.
(8) Loop, M.; Payn, A.; Kanger, T.; Pehk, T. *Tetrahedron Lett.* **1996**, *37*, 7583.
(9) (a) Finn, M. G.; Sharpless, K. B. In *Asymmetric Synthesis*, Vol. 5; Morrison, J. D., Ed.; Academic Press: Orlando, 1995; pp 247−308. (b) Ikegami, S.; Katsuki, T.; Yamaguchi, M. *Chem. Lett.* **1987**, 83. (c) Rossiter, B. E.; Sharpless, K. B. *J. Org. Chem.* **1984**, *49*, 3707
(10) The only other available direct comparison between Ti(IV) and Zr(IV)/tartrate catalysts concerns the asymmetric epoxidation of (*Z*)-hex-3-enol. The two systems afford the 3*R*,4*S* epoxide, respectively with ee's = 50% [ref 9c] and 31% [ref 9b] (30% and 7% chemical yields).
(11) (a) Nugent, W. A.; RajanBabu, T. V.; Burk, M. J. *Science* **1993**, *259*, 479. (b) Nugent, W. A.; Harlow, R. L. *J. Am. Chem. Soc.* **1994**, *116*, 6142.
(12) For a recent review on C_3 symmetric chiral ligands see: Moberg, C. *Angew. Chem., Int. Ed.* **1998**, *37*, 248.
(13) Bonchio, M.; Licini, G.; Modena, G.; Moro, S.; Bortolini, O.; Traldi, P.; Nugent, W. A. *Chem. Commun.* **1997**, 869.
(14) Bonchio, M.; Di Furia, F.; Licini, G.; Modena, G.; Moro, S.; Nugent, W. A. *J. Am. Chem. Soc.* **1997**, *119*, 6935.
(15) Nugent, W.; Licini, G.; Bonchio, M.; Bortolini, O.; Finn, M. G.; McCleland, B. W. *Pure Appl. Chem.* **1998**, *70*, 1041.

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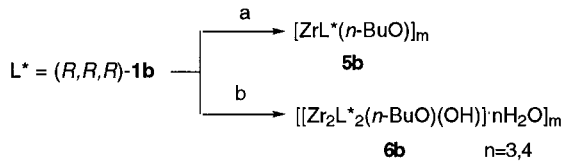
Scheme 2[a]



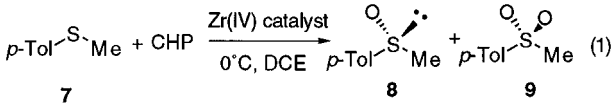
[a] Reagents and conditions: (a) Zr(*n*-BuO)$_4$ (1 equiv), DCE, 20 °C; (b) i. H_2O (2.5 equiv), N_2, CH_2Cl_2, 20 °C; ii. solvent removal; iii. Zr(*n*-BuO)$_4$ (1 equiv), CH_2Cl_2, 20 °C, iv. solvent removal; v. hexane stripping.

n-butyl, or isopropyl aryl sulfoxides, can be obtained with high ee's by direct asymmetric oxidation.[16]

Results and Discussion

The Zr(IV) catalyst **5b** was first prepared in situ under anhydrous conditions (Scheme 2, path a), by reacting Zr(*n*-BuO)$_4$ with **1b** using the same protocol developed for the analogous Ti(IV) system **2b** (Scheme 1, path a).[7]

System **5b** showed little catalytic activity. Oxidation of the model substrate methyl *p*-tolylsulfide **7** (1.08 M) by CHP (0.054 M) in the presence of **5b** (0.0054 M) (eq 1) proceeded slowly (10% conversion of the oxidant in 4 h), affording (*R*)-methyl-*p*-tolyl sulfoxide **8** in low enantiomeric excesses (23%). Furthermore, despite the large excess of the starting sulfide (20 equiv) with respect to the oxidant, a significant amount of the corresponding sulfone **9** was also obtained (**8**:**9** = 80:20). Worthy of notice is the reversed sense of asymmetric induction exhibited by **5b** as compared to the analogous Ti(IV) system **2b**. Thus, in reactions employing the same ligand (*R*,*R*,*R*)-**1b**, Zr (IV) and Ti(IV) catalysts lead to the preferential formation respectively of (*R*)-**8** and (*S*)-**8** sulfoxide.



Therefore, the stereoselection of the oxidation can be controlled by the choice of group 4 metal. This behavior, which has been also observed for the asymmetric epoxidation of allylic alcohols by Ti(IV) and Zr(IV)/tartrate ester complexes,[9a] must be understood in terms of the structure of the active metal species in solution.

Previous studies on the interaction of ligands **1** with Ti(IV) and Zr(IV) alkoxides have shown that while the former affords monomeric complexes, in the case of zirconium, polynuclear aggregates are produced in solution.[11,15,17] In this light, the inversion of the stereochemical outcome of the Zr(IV)-mediated oxidation can likely be ascribed to a change of the geometry of the chiral metal catalyst induced by the aggregation phenomenon.[18]

Since the polynuclear nature of the catalyst seemed to have a strong influence on the stereochemical outcome of the oxidation, the Zr(IV)/**1b** catalytic system was tested under nonanhydrous conditions so as to promote the self-aggregation of the chiral zirconium species in the presence of water.[17] In many cases hydrolyzed alkoxides of early transition metals have shown an improved catalytic activity and selectivity.[6a,f,11,15] Indeed, both the reactivity and enantioselectivity of the Zr(IV)-based system were significantly enhanced by the addition of traces of water to the reaction mixture (eq 1).[19] With this modification, conversion to products was complete in 4 h and (*R*)-**8** was obtained in 49% ee (**8**:**9** = 76:24). We ascribed this result to the formation of a partially hydrolyzed Zr(IV) polynuclear complex which then becomes the active catalyst. To verify this hypothesis, the partially hydrolyzed catalyst **6b** was prepared by reacting a stoichiometric amount of ligand **1b** with Zr(*n*-BuO)$_4$ in the presence of 2.5 equiv of water (Scheme 2, path b). While a detailed study on the hydrolysis conditions (equivalents of water, rate of addition, concentration of the reagents, etc.) is currently under investigation, preliminary results indicate that a stoichiometric amount of water affords a poorly reactive catalyst, behaving similarly to the anhydrous system **5b,** whereas an excess of water (13 equiv) provides a complex that is only slightly soluble in the reaction medium.

Table 1. 6b-Catalyzed Oxidation of Methyl-*p*-tolylsulfide 7 by CHP[a]

entry no.	[**6b**][b] (M)	catalyst (%)	time (h)	conv (%)[c,d]	**8**:**9**[d]	ee (%)[e]
1	0.095	10	3	100	35:65	86 (*R*)
2	0.046	4	5	100	25:75	86 (*R*)
3	0.022	2	18	100	30:70	85 (*R*)
4	0.022	2	3	23	80:20	66 (*R*)
5	0.010	1	21	46	80:20	40 (*R*)
6	0.005	0.5	21	26	100:0	9 (*R*)
7	0.0005	0.05	27	18	100:0	1 (*S*)

[a] $[\mathbf{7}]_0$ = [CHP] = 1.08 M, in DCE at 0 °C. [b] Calculated per Zr atom. [c] Conversions based on the oxidant and calculated as conv. = ([**8**] + 2[**9**])/$[CHP]_0$. [d] Determined by GC analysis. [e] Determined by HPLC analysis.

The procedure described in Scheme 2, path b, affords a white powder which reproducibly analyzes according to the minimal formula **6b** (see Experimental Section). Indeed, complex **6b** effectively catalyzes the oxidation of **7** (100% conversion in 4 h, 44% ee, (*R*), **8**:**9** = 76:24) *without the requirement for extra water addition*.

Optimization of the reaction conditions, namely, catalyst and substrate concentrations, temperature, order of addition of reagents, etc., allowed us to improve the enantioselectivity of this process up to 86% (Table 1).

We discovered that such high enantioselectivity could be achieved using only 2% of catalyst **6b**, provided that [**6b**] > 0.02 M. The data of Table 1, in particular the constancy of the ee's and of the product distribution for entries 1−3, suggest that this concentration limit is critical to the stability of the chiral Zr(IV) active species. In fact, both a reduced catalytic activity and a lower enantioselectivity were obtained at [**6b**] = 0.01 M (compare entries 4 and 5 at equal product distribution). For [**6b**] ≤ 0.005 M also the chemoselectivity of the oxidation changes dramatically (compare, for analogous conversion of the oxidant, the product distributions in entries 4 and 6), consistent with a major structural modification of the active catalyst. Moreover when a sub-millimolar concentration of **6b** is used (entry 7), a reversal in the sense of asymmetric induction in the oxidation of **7** is observed.

(16) Compare for example the ee's obtained for the analogous substrates with the Kagan protocol which are 7, 34, 20, and 63%, respectively. Pitchen, P.; Dunãch, E.; Deshmukh, M. N.; Kagan, H. B. *J. Am. Chem. Soc.* **1984**, *106*, 8188.

(17) Nugent, W. A. *J. Am. Chem. Soc.* **1992**, *114*, 2768.

(18) A similar argument has been used to address the behavior of Mg(II)/chiral bis(oxazoline) catalysts: Desimoni, G.; Faita, G.; Gamba Invernizzi, A.; Righetti, P. *Tetrahedron* **1997**, *53*, 7671.

(19) The model reaction was performed by adding to the reaction mixture (1 mL) a saturated solution of water in 1,2-dichloroethane (20 μL).

Table 2. 6a−c-Catalyzed Oxidation of Methyl-*p*-tolylsulfide 7 by CHP[a]

entry no.	ligand	time (h)	conv (%)[b,c]	**8**:**9**[c]	ee (%)[d]
1	(*S*,*S*,*S*)-**1a**	48	72	54:46	10 (*S*)
2	(*R*,*R*,*R*)-**1b**	5	100	25:75	86 (*R*)
3	(*R*,*R*,*R*)-**1c**	26	100	30:70	9 (*R*)

[a] $[\mathbf{7}]_0$ = [CHP] = 1.08 M, [**6a**] = 0.1 M per Zr atom, [**6b**] = [**6c**] = 0.022 M per Zr atom, in DCE at 0 °C. [b] Conversions based on the oxidant and calculated as conv. = ([**8**] + 2[**9**])/$[\mathrm{CHP}]_0$. [c] Determined by GC analysis. [d] Determined by HPLC analysis.

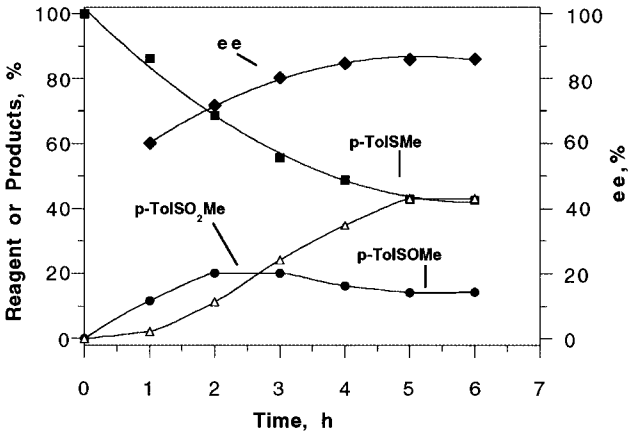


Figure 1. Plot of reagent, products (%), and ee (%) vs time (h) in the oxidation of **7** (1.08 M) with CHP [1.08 M] catalyzed by **6b** (4.4×10^{-2} M) in DCE at 0 °C.

Thus, in the system under examination, at high dilution and under high turnover conditions (TO > 200), both the reactivity (reduced overoxidation to sulfone) and the sense of stereoselection parallel those observed with the monomeric Ti(IV) complex **4**.[7,14,15] Taken as a whole, these experimental observations indicate that the excess of the hydroperoxide affects the solution integrity and in particular the degree of oligomerization of the active Zr(IV) species.

The influence of the chiral ligand **1** on the reactivity and enantioselectivity of the hydrolyzed catalysts **6** is illustrated in Table 2.

As already observed in the Ti(IV)-mediated oxidations, also in the case of the Zr(IV) system ligand **1b** affords a catalyst with superior performance.

The kinetic profile for the oxidation of **7** by CHP in the presence of **6b** (Figure 1) provides insight into the course of the reaction. Two consecutive reactions take place, namely, the oxidation of the sulfide to the sulfoxide and a subsequent second oxygen transfer to yield the corresponding sulfone. The time variation of the sulfoxide concentration, which goes through a maximum for $t = 2$ h, indicates that the oxygen transfer to sulfoxide is the faster of the two oxidative processes.[20]

Indeed, two independent stereoselective processes occur in solution:[21] the asymmetric oxidation producing methyl *p*-tolyl sulfoxide **8** and its subsequent kinetic resolution[22] via further oxidation to sulfone. It should be noted that the ee of the sulfoxide steadily increases during the reaction. This indicates that both processes cooperate in building up the same enantiomer. This proposal is directly supported by the analysis of the kinetic resolution of the (±)-**8** catalyzed by **6b**, where (*R*)-**8** can be recovered with ee up to 93% (Figure 2).

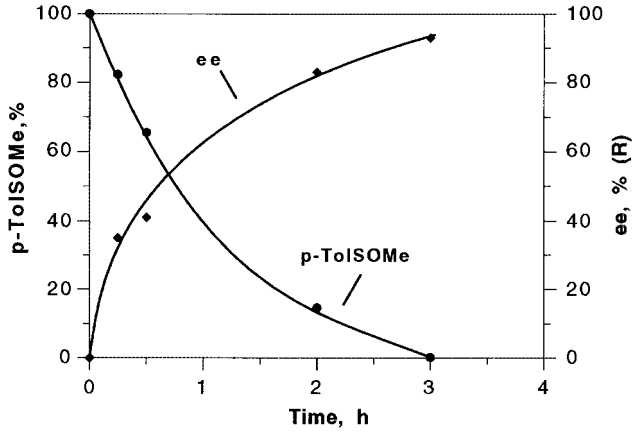


Figure 2. Plot of reagent (%) and ee (%) vs time (h) in the oxidation of **(±)-8** (1.08 M) with CHP [1.08 M] catalyzed by **6b** (4.4×10^{-2} M) in DCE at 0 °C.

Table 3. 6b-Catalyzed Stereoselective Oxidation of Alkyl Aryl and Dialkylsulfides by CHP[a]

entry no.	R	R′	time (h)	conv (%)[b]	SO:SO_2[c,e]	ee (%)[e,f]
1	Ph	Me	5	100[c]	29:71[c]	89[f] (*R*)
2	*p*-Me−C_6H_4	Me	5	100[c]	25:75[c]	86[f] (*R*)
3	*p*-MeO−C_6H_4	Me	4	100[d]	32:68[e]	89[e] (*R*)
4	*p*-Cl−C_6H_4	Me	6	100[d]	32:68[e]	86[e] (*R*)
5	2-Naph	Me	6	100[d]	52:48[e]	88[e] (*R*)
6	*p*-Me−C_6H_4	*n*-Bu	6	94[c]	37:63[c]	91[f] (*R*)
7	*p*-Me−C_6H_4	*i*-Pr	21	100[c]	28:72[c]	91[f] (*R*)
8	Ph	*t*-Bu	19	33[c]	44:56[c]	77[f] (*R*)
9	Ph	Bn	6	95[c]	22:78[c]	79[f] (*R*)
10	Bn	Me	2	100[d]	60:40[e]	14[e] (*S*)
11	*n*-Oct	Me	2	100[d]	60:40[e]	8[e] (*S*)

[a] Reaction conditions: $[\text{substrate}]_0 = [\mathrm{CHP}]_0 = 1.08$ M, [**6b**] = 4.6×10^{-2} M per Zr atom in DCE at 0 °C. [b] Conversions based on the oxidant and calculated as conv. = ([**SO**] + 2[$\mathbf{SO_2}$])/$[\mathrm{CHP}]_0$. [c] Determined by GC analysis. [d] Determined on the isolated products. [e] Determined by ^{1}H NMR analysis. [f] Determined by HPLC analysis.

It is noteworthy that, compared with the Ti(IV)/**1b**/CHP system,[7] the Zr(IV) catalyst affords higher enantioselectivity in both oxidation steps.[23] The cooperative effect of asymmetric oxidation and kinetic resolution provides a useful strategy for obtaining sulfoxides with high ee's from processes that are moderately stereoselective,[21,24] although causing an ineluctable depletion of the chemical yields of the product of interest.

The scope of the Zr(IV)-based enantioselective sulfoxidation is revealed in Table 3.

The method appears to be fairly general for the alkyl aryl sulfides since ee's in the range 80−90% are obtained

(20) This observation, which may reflect a metal-promoted nucleophilic oxidation of the sulfinyl moiety (see ref 14), is currently under investigation.

(21) For other stereoselective sulfoxidations involving cooperative asymmetric oxidation and kinetic resolution see: Komatsu, N.; Hashizume, M.; Sugita, T.; Uemura, S. *J. Org. Chem.* **1993**, *58*, 4529. Nagata, T.; Imagawa, K.; Yamada, T.; Mukaiama, T. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 3241. Adam, W.; Korb, M. N.; Roschmann, K. J.; Saha-Möller. *J. Org. Chem.* **1998**, *63*, 3423, and references 6e, 7.

(22) Komatsu, N.; Hashizume, M.; Sugita, T.; Uemura, S. *J. Org. Chem.* **1993**, *58*, 7624. Scettri, A.; Bonadies, F.; Lattanzi, A.; Senatore, A.; Soriente, A. *Tetrahedron: Asymmetry* **1996**, *6*, 657.

(23) As an example, in the oxidation of **7** at product distribution **8**:**9** = 84:16, **6b** and **2b** systems afford ee's of 60% and 33%, respectively. Likewise, kinetic resolution of (±)-**8** at 35% conversion provides ee's of 41% and 22%, respectively.

(24) Krontil, W.; Kleewein, A.; Faber, K. *Tetrahedron: Asymmetry* **1997**, *8*, 3251.

for the oxidation of a variety of substrates with different stereoelectronic features. Neither the presence of aromatic substituents with diverse electronic character (entries 1−4) nor substitution with a 2-naphthyl group (entry 5) has a meaningful effect on the enantioselecitivity of the process. Likewise, enantioselectivity is not significantly diminished by elongation (entry 6) or increased bulkiness (entries 7−9) of the alkyl substituent. The latter observation stands in contrast to previously reported metal-mediated sulfoxidation reactions where a significant steric differentiation between the two residues linked to the sulfur atom is typically required for high enantioselectivity.[6a,16] On the other hand, dialkylsulfides (entries 10 and 11) afford the corresponding sulfoxides in very low ee's and with the opposite absolute configuration. Therefore, inspection of data reported in Table 2 seems to indicate that the molecular recognition mechanism of the chiral Zr(IV) oxidant operates through noncovalent aromatic interactions (edge to face or face to face) with the substrate.[7,25] Although further investigation will be required to substantiate this hypothesis, it should be noted that poor enantioselectivities are indeed observed only for sulfides lacking the aromatic substituent. Studies aimed at elucidating both the catalyst structure and the reaction mechanism as well as at extending the scope of the Zr(IV)/**1b**-based system are currently being pursued.

Experimental Section

General Methods. ^{1}H NMR spectra were recorded on a Bruker AC-200 SY (200 MHz) or a AC-250 (250 MHz) instrument. Helium fast atom bombardment (FAB) mass spectra were collected on a single quadrupole instrument (HP-ENGINE). The helium atom gun was operated at an accelerating voltage of 8 kV and heating current of 10 μA. Test samples were prepared by dissolving the complex under investigation (0.1 mg) in 3-nitrobenzyl alcohol (NBA) used as the liquid matrix. Enantiomeric excesses were determined directly on reaction mixtures by HPLC analysis performed on a Water-Associates HPLC/GPC (FDP) 201 pump and a Water-Associates 440 UV detector (λ = 254 nm) with a Lichrosorb S100 CSP-DACH-DNB [(250 × 4.0 mm (i.d.)] chiral column[26] with *n*-hexane/2-propanol (8:2) as eluent, flow rate of 1.6 mL/min, P = 800 psi, reactions with *p*-Tol-S-Me, *p*-Tol-S-*n*-Bu Ph-S-*t*-Bu, *p*-Tol-S-*i*-Pr; flow rate of 0.9 mL/min, P = 700 psi, reaction with Me-S-*n*-Oct; flow rate of 2.0 mL/min, P = 1000 psi, reaction with Ph-S-Bn. For the other substrates, sulfoxide ee's were determined directly on the crude product mixture by ^{1}H NMR in the presence of (*R*)-(−)-1-(9-anthryl)-2,2,2-trifluoroethanol[27] (Fluka). Absolute configurations were assigned via HPLC analysis according to the elution order on a (*S*,*S*)-CSP-DACH-DNB chiral column[26] in which the (*S*) enantiomer of the selected sulfoxides is eluted before the (*R*) one, and/or via ^{1}H NMR in the presence of (*R*)-(−)-1-(9-anthryl)-2,2,2-trifluoroethanol[27] by comparison of authentic samples with known configuration[7,28] (see Tables 1−3). Gas-chromatographic analyses were performed using a Varian 3700 GC equipped with a 0.5m × 2 mm glass column packed with 3% FFAP on Chromosorb WAW DMCS (80−100 mesh) or a Hewlett-Packard 5890 Series II GC equipped with a SE-30 15 m × 0.25 mm (i.d.) capillary column.

Chemicals. Dichloromethane was distilled over CaH_2 and stored over molecular sieves. 1,2-Dichloroethane (DCE) was washed three times with 10% concentrated H_2SO_4 and with water several times until a pH of 7, dried over $CaCl_2$ overnight, distilled over P_2O_5, and stored over molecular sieves. Cumyl hydroperoxide (80% in cumene, Fluka) was stored over molecular sieves at 0 °C. Zirconium tetra-*n*-butoxide (80% in *n*-butanol, Aldrich) was stored under nitrogen. Sulfides were prepared accordingly to literature by alkylation of the corresponding sodium arylthiolates.[29] Enantiopure trialkanolamines **1** were prepared following the literature procedure.[11b]

Synthesis of Catalyst 6b. Ligand **1b** (46 mg, 0.12 mmol) was dissolved in dry dichloromethane (3 mL) under nitrogen and magnetic stirring. Water (5.7 μL, 0.32 mmol) was added and the solvent removed under reduced pressure (12 mmHg). After addition of dry dichloromethane (3 mL), zirconium(IV) tetra-*n*-butoxide (80% in *n*-BuOH, 50 μL, 0.11 mmol) was added. The solution was stirred for 15 min, then the solvent was removed under reduced pressure. The recovered material was dissolved in dichloromethane (3 mL), and the solvent was removed again under vacuum. After washing with hexane (6 mL), the solvent was removed under vacuum, yielding a white solid (61 mg) that was dried under high vacuum (0.1 mmHg) for 1 h and stored under nitrogen. **6b** ^{1}H NMR shows a complex and well-resolved spectrum consistent with the presence of a major species being a stable nonsymmetric aggregate in which **1b** and *n*-BuO are present in a 2:1 molar ratio (see Supporting Information). Despite the complexity of the spectrum, different signals corresponding to the different set of protons can be recognized as follows. ^{1}H NMR ($CDCl_3$), δ (ppm): 0.82 (3H, t, J = 7.2 Hz); 1.16−1.47 (4H, m); 2.43−3.60 (18H, m); 4.73 (1H, t, J = 4.7 Hz); 5.14−6.13 (6H, m); 6.43 (2H, m); 6.87−8.10 (28−35H, m). On the basis of ^{1}H NMR evidence and elemental analyses the minimal formula $[Zr_2(N(CH_2CHPhO)_3)_2(n\text{-BuO})(OH)]\cdot nH_2O$, n = 3 or 4, can be proposed for catalyst **6b**. Different batches of catalyst **6b**, displaying analogous reactivity, afforded elemental analysis consistent with the empirical composition reported above. Two representative elemental analyses are as follows: for n = 3, MW = 1075.5. Anal. Calcd for $C_{52}H_{64}N_2O_{11}Zr_2$: C, 58.07; H, 6.00; N, 2.60. Found: C, 58.30; H, 5.42; N, 2.56. For n = 4, MW = 1093.5. Anal. Calcd for $C_{52}H_{66}N_2O_{12}Zr_2$: C, 57.11; H, 6.08; N, 2.56. Found: C, 57.11; H, 5.76; N, 2.44.

FAB MS data (%) (NBA): 1096 (14); 1078 (23); 973 (13); 843 (15); 735 (17); 586 (35); 464 (67); 413 (55); 351 (96); 242 (100).

Partially hydrolyzed zirconium catalysts **6a** and **6c,** bearing ligands **1a** and **1c** respectively, have been synthesized following the procedure described above. In both cases highly hygroscopic, vitreous white solids were obtained, whose catalytic activity have been tested without further characterization.

General Procedure for the Asymmetric Sulfoxidation. In a Schlenck apparatus, under nitrogen and with magnetic stirring, catalyst **6b** (14.3 mg, 0.027 mmol) and eventually an internal standard were dissolved in 0.5 mL of dry DCE. After cooling at 0 °C, cumyl hydroperoxide (0.100 mL, 0.54 mmol) and, after 1 h, the sulfide (0.54 mmol) were subsequently added. The reaction was monitored via GC and HPLC, after quenching the hydroperoxide with triphenylphosphine or di-*n*-butylsulfide. The homogeneous and colorless solution was stirred at 0 °C until complete consumption of the oxidant (iodometric test), warmed at room temperature, and poured into a 5% sodium metabisulfite aqueous solution. The mixture was extracted with chloroform, the organic layers were washed with brine and dried over $MgSO_4$, and the solvent was removed under vacuum. Yields were determined via quantitative GC analysis or on product isolation and product distributions via quantitative GC analysis or ^{1}H NMR (see Tables 1−3). Products were purified via radial chromatography over silica gel (petroleum ether/ethyl acetate). The sulfoxides and sulfones spectral data match those already

(25) For a recent discussion on chiral molecular recognition mechanisms based either on steric destabilization of the pathway leading to the minor enantiomer or stabilization via secondary catalyst−substrate interaction of the transition state producing the major enantiomer see: Quan, R. W.; Li, Z.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1996**, *118*, 8156.

(26) (a) Gargano, G.; Gasparrini, F.; Misiti, D.; Palmieri, G.; Pierini, M.; Villani, C. *Chromatographia* **1987**, *24*, 505. (b) Altomare, C.; Carotti, A.; Cellamare, S.; Fanelli, F.; Gasparrini, F.; Villani, C.; Carrupt P.-A.; Testa, B. *Chirality* **1993**, *5*, 527.

(27) (a) Pirkle, W. H.; Beare, S. D. *J. Am. Chem. Soc.* **1968**, *90*, 6250. (b) Pirkle, W. H.; Hoover, D. J. *Top. Stereochem.* **1982**, *13*, 263−331.

(28) (a) Brunel, J. M.; Diter, P.; Duetsch, M.; Kagan, H. B. *J. Org. Chem.* **1995**, *60*, 8086. (b) Rebiere, F.; Samuel, O.; Ricard, L.; Kagan, H. B. *J. Org. Chem.* **1991**, *56*, 5991, and references therein.

(29) Peach, M. E. In *The Chemistry of Thiol Group, Part 2*; Patai, S., Ed.; John Wiley & Sons, Ltd.: Bristol, England, 1974; Chapter 16, pp 721−784.

reported.[7,16,28] Ee's were determined directly on the reaction mixture before purification by chiral HPLC[28] or by ^{1}H NMR in the presence of (*R*)-(−)-1-(9-anthryl)-2,2,2-trifluoroethanol.[27]

Procedure for the Kinetic Study of the Stereoselective Oxidation of Methyl-*p*-Tolylsulfide (7) and the Kinetic Resolution of (±)-Methyl-*p*-Tolyl Sulfoxide (8). The reaction solutions were prepared as described above using 1,3,5-trichlorobenzene as internal standard. At the reaction times stated in Figures 1 and 2, two samples of the mixture (0.025 mL) were taken out and immediately quenched with an excess of triphenylphosphine, for the determination of conversion and product distribution (GC analysis), and di-*n*-butylsulfide for the ee determination of **8** (HPLC analysis).

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Supporting Information Available: ^{1}H NMR ($CDCl_3$) of **6b** (1 page). See any current masthead page for ordering information.

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