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Investigations on the Iron-Catalyzed Asymmetric Sulfide Oxidation

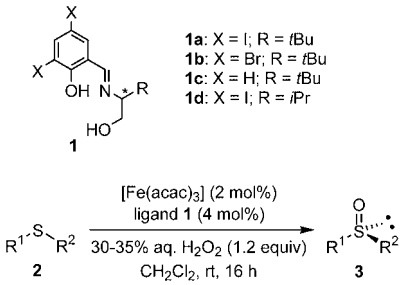
Julien Legros and Carsten Bolm*[a]

Abstract: The development of an enantioselective sulfide oxidation involving a chiral iron catalyst and aqueous hydrogen peroxide as oxidant is described. In the presence of a simple carboxylic acid, or a carboxylate salt, the reaction affords sulfoxides with remarkable enantioselectivities (up to 96% *ee*) in moderate to good yields. The influence of the structure of the additive on the reaction outcome is reported. In the sulfoxide-to-sulfone oxidation a kinetic resolution (with $s=$ 4.8) occurs, which, however, plays only a negligible role in the overall enantioselective process. Furthermore, a positive nonlinear relationship between the *ee* of the product and that of the catalyst has been found. On the basis of these observations, a possible catalyst structure is proposed.

Keywords: asymmetric amplification · asymmetric catalysis · iron · oxidation · sulfoxide

Introduction

Chiral sulfoxides find increasing use as auxiliaries in asymmetric synthesis and ligands in enantioselective catalysis,[1] and recently, they have been shown to promote asymmetric allylation reactions.[2] Moreover, a number of pharmaceutically important drugs contain asymmetric sulfinyl moieties.[1a,3] The development of processes for the preparation of chiral sulfoxides with high enantiomeric purity is therefore a prime target. Among all methods described so far, the asymmetric oxidation of sulfides by metal catalysts is one of the most attractive routes to optically active sulfoxides.[4] In this line, titanium, manganese and vanadium complexes have been widely applied.[4,5] Conversely, catalysts based on nontoxic and inexpensive iron is relatively underrepresented in the field,[6] and the few systems developed so far fail in terms of efficiency and practicability.[7] Most of them involve structurally complex iron porphyrines, and iodosylbenzene or alkyl hydroperoxides as terminal oxidant, and, most importantly, the enantioselectivities are only moderate (<55% *ee*).[7a–e] The iron complex $[Fe_2O(pb)_4(H_2O)_2](ClO_4)_4$ (pb = (−)-4,5-pinene-2,2′-bipyridine) was reported by Fontecave et al. as catalyst for the sulfide oxidation with H_2O_2, but the enantioselectivity remained rather low ($ee_{max}=40\%$).[7f–h] Consequently, finding an efficient iron-catalyzed asymmetric sulfoxidation reaction, which proceeds under mild reaction conditions, still remains an attractive goal. In this context, we recently reported on a novel iron-catalyzed asymmetric sulfide oxidation that fulfils most of the requirements and affords sulfoxides with up to 90% *ee*.[8] It proceeds under very simple reactions conditions (at room temperature in a capped flask) and utilizes (≤4 mol% of) a readily available chiral iron complex, generated in situ from $[Fe(acac)_3]$ and a Schiff base ligand of type **1**.[9] Furthermore, inexpensive and safe 35% aqueous hydrogen peroxide[10] serves as terminal oxidant (Scheme 1).



Scheme 1.

A limitation of the reported iron catalysis stemmed from the fact that under the conditions required for achieving high enantioselectivities, large amounts of unreacted substrates remained, limiting the sulfoxide yields (≤44%). In a subsequent communication we then disclosed that the effi-

[a] Dr. J. Legros, Prof. Dr. C. Bolm
Institut für Organische Chemie
Rheinisch-Westfälische Technische Hochschule
Professor-Pirlet-Strasse 1, 52056 Aachen (Germany)
Fax: (+49) 241-809-2391
E-mail: carsten.bolm@oc.rwth-aachen.de

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ciency of the process (in terms of both enantioselectivity and yield) could greatly be improved by using additives.[11] We now detail the influence of the additive structure on the reaction course and describe further investigations revealing specific features of this novel iron-catalyzed process.

Results and Discussion

The use of additives is a common and convenient method for the efficiency enhancement of metal-catalyzed reactions.[12] They facilitate catalyst tuning without re-designing the ligand, and very often their value is under-appreciated. Unfortunately, the process of discovering which additive has to be used clearly requires trial and error and can commonly not be predicted. In asymmetric sulfoxidation, this strategy has already been applied. For example, Maruyama and Naruta used 1-methylimidazole in catalyses with iron porphyrins,[7b,c] and in Bolm's vanadium-catalyzed process,[9] Katsuki et al. added methanol in order to improve the enantioselectivity (without affecting the catalyst turnover and yield).[9e] Our attempts to use those additives in the iron-catalyzed reaction shown in Scheme 1 led to clearly negative effects. In epoxidation reactions with H_2O_2 catalyzed by iron complex $[Fe^{II}(mep)(CH_3CN)_2](SbF_6)_2$ (mep = *N*,*N*′-dimethyl-*N*,*N*′-bis(2-pyridylmethyl)-ethane, 1,2-diamine) Jacobsen recently found that the presence of sub-stoichiometric amounts of a carboxylic acid stabilized the catalytic system making it more well-behaved improving its efficiency. Consequently, even with a reduced catalyst loading and an increased H_2O_2 addition rate (from dropwise to rapid addition) higher epoxide yields were achieved.[13] These results suggested an investigation of the iron-catalyzed sulfoxidation (Scheme 1) with benzoic acid (**AH1**) as additive. Thioanisole (**2a**) was selected as substrate, and the catalyses were performed with (*S*)-**1a** as ligand under the previously optimized reaction conditions. The effect of the acid on the behavior of the catalyst system was remarkable. It appeared to be entirely dependent on the additive quantity, and the best enantioselectivity was obtained with an **AH1**/[Fe(acac)$_3$] ratio of 0.5:1. Under those conditions, the *ee* of the corresponding sulfoxide **3a** increased from 59% (no additive) to 73% (Figure 1). Gratifyingly, the yield of **3a** was also higher than before (56% versus 41% without the additive). Increasing the **AH1**/[Fe(acac)$_3$] ratio to 10:1 had almost no effect on the yield of the sulfoxide (71%), but lowered the *ee* of **3a** to only 9%.

The electronic and steric properties of the additive were easily fine-tuned by using various commercially available substituted benzoic acids. This screening, which was done under optimized conditions (with 0.5 equivalents of the additive relative to [Fe(acac)$_3$]), was extended to the use of nonaromatic additives (Figure 2).

The reaction outcome was highly dependent on the nature and the position of the substituents on the aryl ring. With electron-withdrawing groups (NO_2, **AH2**–**AH4**; I, **AH5**), a decrease of the catalysis efficiency [compared with the one with benzoic acid (**AH1**)] was observed. In contrast, use of *para*-substituted electron rich derivatives **AH6** (*p*Me_2N) and **AH7** (*p*MeO) led to very good results, affording **3a** with 80% *ee* in 68 and 66% yield, respectively. Sterically hindered acids **AH10**–**12** gave good results (74–79% *ee*) as well. Nonconjugated acids [acetic acid (**AH1**) and phenylacetic acid (**AH14**)] have also been assessed and showed improvements with respect to the initial conditions, but the enantioselectivity remained inferior (70% *ee*). Chiral acids, (*R*)- and (*S*)-mandelic acid (**AH15** and **AH16**) and their corresponding methyl derivatives (**AH17** and **AH18**) were totally ineffective.

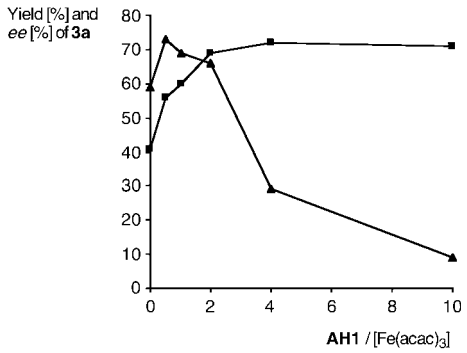


Figure 1. Effect of benzoic acid (**AH1**) on the *ee* (measured on the crude; ▲) and yield (NMR yield; ■) of (*S*)-**3a** in the asymmetric oxidation of **2a** with 35% H_2O_2 (1.2 equiv) catalyzed by [Fe(acac)$_3$] (2 mol%) and (*S*)-**1a** (4 mol%).

Next, benzoic acid derivative **AH7** was studied in combination with catalysts based on other Schiff bases (Table 1). A positive effect was also observed with Schiff base **1b** (entries 3 and 4) leading to major improvements in yield and enantioselectivity, very close to the ones obtained with **1a**. Only a modest increase of the enantioselectivity was observed with **1c** (entries 5 and 6). Schiff base **1d** derived from valinol had no effect on both yield and *ee* (entries 7 and 8).

The halogen atoms on the aromatic ring (I, **1a**; Br, **1b**) and the *tert*-butyl group (stemming from *tert*-leucinol) in the imino alcohol side chain of the ligand have a tremendous influence on the reaction outcome. Whereas we have no rational explanation for this "halogen effect" at this time, it is interesting to note that **1a** is also optimal in the related vanadium-catalyzed sulfoxidation process.[9d] Conversely, Schiff base **1b** is much less efficient in this latter system.[14]

Next, we once more focussed our attention on the additive structure. The fact, that electron rich carboxylic acids (**AH6**, **AH7**) led to the best results suggested that the additive acted as a co-ligand and that its chelating property and not its acidity was the essential point. It was therefore hypothesized that a carboxylate salt should further increase the efficiency of the reaction. Lithium, sodium, potassium, cesium and tetrabutylammonium 4-methoxybenzoates (**ALi7**, **ANa7**, **AK7**, **ACs7** and **ABu$_4$N7**, respectively) were thus assessed in the oxidation of **2a** by using Schiff base **1a** as ligand (Table 2). Confirming our assumption we found

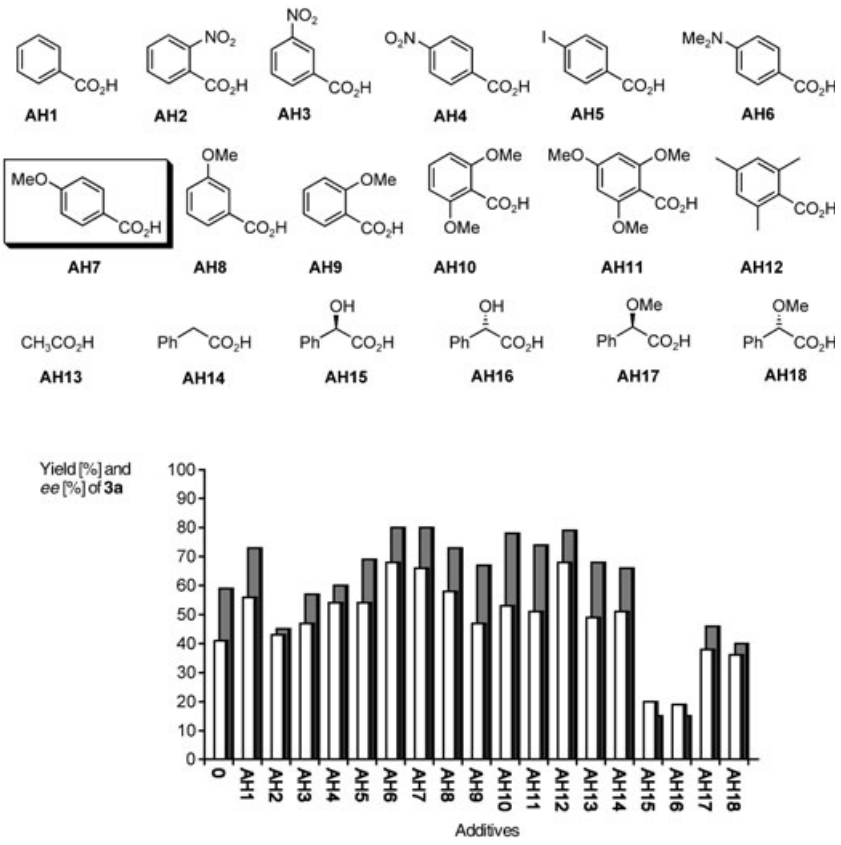


Figure 2. Influence of various carboxylic acids (**AH1**–**AH18**; 1 mol%) on the yield (NMR yield; clear, front) and the *ee* (measured on the crude; dark, back) of (*S*)-**3a** in the asymmetric oxidation of **2a** with 35% H_2O_2 (1.2 equiv) catalyzed by [Fe(acac)$_3$] (2 mol%) and (*S*)-**1a** (4 mol%).

Table 1. Catalytic enantioselective oxidation of **2a** with H_2O_2 and a chiral iron complex in presence of **AH7**.[a]

Entry	Ligand (*S*)-**1**	**AH7**	Yield **3a** [%][b]	*ee* **3a** [%][c]
1	**1a**	–	36	59
2		+	63	80
3	**1b**	–	30	55
4		+	53	80
5	**1c**	–	27	26
6		+	27	43
7	**1d**	–	50	22
8		+	53	24

[a] Reaction conditions: [Fe(acac)$_3$] (0.02 mmol), (*S*)-**1** (0.04 mmol), (**AH7**; 0.01 mmol), **2a** (1 mmol) and aqueous H_2O_2 (35%; 1.2 mmol) in CH_2Cl_2 at room temperature for 16 h. [b] Yield of isolated product. [c] The enantiomer ratios were determined by HPLC using a chiral stationary phase. **3a** had (*S*) configuration in all cases.

that all the metal salts (entries 2–5) gave improved results with enantioselectivities of up to 90% *ee* for **ALi7** and **ANa7** (entries 2 and 3, respectively). The yields of **3a** were comparable in all reactions.

The substrate scope was then studied under optimized conditions (Table 3).

For all substrates assessed the presence of **AH7** and **ALi7** greatly improved both enantioselectivity and yield. Whereas 44% was the best yield under the previous conditions without the additive, almost all sulfoxides were now obtained in more than 55% yield.[8] In terms of asymmetric induction the best results were obtained with phenyl methyl sulfide (**2a**) and *para*-substituted derivatives thereof, where all sulfoxides had *ee* values above 90% (ee_{max} = 96%). The oxidations of more challenging substrates like phenyl ethyl sulfide (**3b**: 82% *ee*, 56% yield) and phenyl benzyl sulfide (**3c**: 79% *ee*, 73% yield) proceeded remarkably well too. For the last substrate, the improvement due to the additive was particularly impressive (no additive: 27% *ee*, 44% yield). It is worth to note also that, without any additive, only sulfoxide **3h** was previously obtained with an *ee* superior to 80%. Interestingly, with vinyl- and allyl phenyl sulfides (**2m** and **2n**, respectively), the reaction was highly chemoselective affording only sulfoxides **3m** and **3n** with good enantioselectivities (>70% *ee*).

Table 2. Catalytic enantioselective oxidation of **2a** with H_2O_2, [Fe(acac)$_3$] and Schiff base **1a**, in presence of **AX7**.[a]

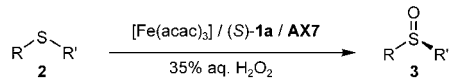
Entry	**AX7** (X=)	Yield of **3a** [%][b]	*ee* of **3a** [%][c]
1	H	63	80
2	Li	63	90
3	Na	67	90
4	K	64	88
5	Cs	65	87
6	Bu_4N	57	82

[a]–[c] As in Table 1.

An oxidation of the double bond was not observed. As a general feature, the reaction proceeded with high enantioselectivity for a wide variety of monoaryl sulfides. Assessment of other substrate types gave, for the moment, unsatisfactory results (e.g. Bn-S(O)-Me **3o**: 23% *ee*, 64% yield).[15]

Kinetic resolution: The fact that each time, when the reaction afforded a sulfoxide with high *ee* (≥80%), a significant amount of sulfone (9–16%; see Table 3) was detected in the crude product mixture, suggested the existence of a kinetic resolution process during the course of the reaction.[16] In order to investigate this aspect an experiment was performed under standard asymmetric sulfide oxidation condi-

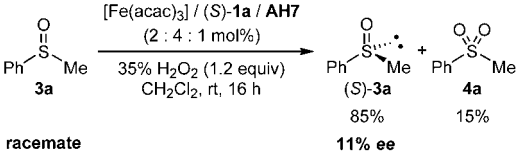
Table 3. Catalytic enantioselective oxidation of sulfides **2** with H_2O_2 and a chiral iron complex in presence of an additive.[a]



Entry	Sulfide **2**			Sulfoxide **3**					
				no additive		with additive			
	R	R′		Yield [%][b]	*ee* [%][c]	**AX7**	Yield [%][b]	*ee* [%][c,d]	
1	Ph	Me	**2a**	36	59	**ALi7**	63	90	**3a**
2[e]	Ph	Me	**2a**	n.p.[f]	n.p.	**ALi7**	64	88	**3a**
3	Ph	Et	**2b**	30	44	**ALi7**	56	82	**3b**
4	Ph	Bn	**2c**	40	27	**AH7**	73	79	**3c**
5	4-MeC_6H_4	Me	**2d**	n.p.	n.p.	**ALi7**	78	92	**3d**
6	4-$MeOC_6H_4$	Me	**2e**	n.p.	n.p.	**ALi7**	66	86	**3e**
7	4-BrC_6H_4	Me	**2f**	41	78	**ALi7**	59	94	**3f**
8	4-ClC_6H_4	Me	**2g**	32	65	**AH7**	60	92	**3g**
9	4-$NO_2C_6H_4$	Me	**2h**	21	90	**ALi7**	36	96	**3h**
10	2-BrC_6H_4	Me	**2i**	n.p.	n.p.	**ALi7**	48	66	**3i**
11	2-$MeOC_6H_4$	Me	**2j**	n.p.	n.p.	**ALi7**	50	70	**3j**
12	mesityl	Me	**2k**	n.p.	n.p.	**ALi7**	44	77	**3k**
13	2-naphthyl	Me	**2l**	44	70	**AH7**	67	95	**3l**
14	Ph	$CH=CH_2$	**2m**	n.p.	n.p.	**ALi7**	34	75	**3m**
15	Ph	$CH_2CH=CH_2$	**2n**	n.p.	n.p.	**ALi7**	63	71	**3n**
16	Bn	Me	**2o**	n.p.	n.p.	**ALi7**	64	23	**3o**

[a] Reaction conditions: [Fe(acac)$_3$] (0.02 mmol), Schiff base (*S*)-**1a** (0.04 mmol), **AH7** or **ALi7** (0.01 mmol), sulfide **2** (1 mmol) and aqueous H_2O_2 (35%; 1.2 mmol) in CH_2Cl_2 at room temperature for 16 h. [b] Yield of isolated product. [c] The enantiomer ratios were determined by HPLC analysis of the isolated product by using a chiral stationary phase. See Experimental Section. [d] Each time the reaction afforded sulfoxide **3** with >80% *ee*, 9–16% of sulfone **4** was detected. [e] Reaction performed with (*R*)-**1a**. [f] Experiment not performed (n.p.).

tions using racemic sulfoxide **3a** as substrate, Schiff base (*S*)-**1a** as ligand and **AH7** as additive (Scheme 2).[17]



Scheme 2.

After 16 h reaction time the conversion of sulfoxide **3a** to sulfone **4a** was low (15%), and a large quantity of **3a** could be recovered. The *ee* of 11% for recovered **3a** (in favor for the *S*-configured sulfoxide) revealed that the sulfoxide-to-sulfone oxidation was indeed enantioselective (with $k_R > k_S$). Even though the stereoselectivity factor (*s*)[18] was rather small (4.8), we decided to study the time dependence of the asymmetric process in more detail. By determining the conversion of thioanisole (**2a**), the formation of sulfoxide **3a**, the enantiomer ratio of **3a**, and the formation of sulfone **4a** with time, we hoped to shine light on the importance of the kinetic resolution for the overall oxidative process (Figure 3).

After 0.5 h reaction time, sulfoxide **3a** was formed in 11% yield (as determined by NMR) having an *ee* of 78%. No sulfone **4a** was detected as this stage. After 16 h, the yield of **3a** was 70%, and the product had 80% *ee*. At this stage 9% of sulfone **4a** were found. Thus, the *ee* of **3a** remained almost constant during the reaction course (78±2%), independent of the formation of **3a** and **4a**. Consequently, it can be concluded that under the experimental conditions applied for the sulfide oxidation, the kinetic resolution plays only a negligible role and that the observed enantioselectivity originates (almost exclusively) from the asymmetric sulfide oxidation itself. Apparently, the kinetic resolution does not significantly affect the *ee* of the sulfoxide.[19]

Nonlinear effect: The search for nonlinear effects (NLE) in a given system has become a useful probe for analyzing the nature of the catalytic species involved in an asymmetric process.[20] With the intention to get

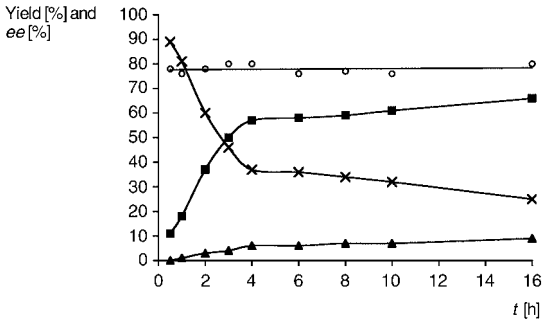


Figure 3. Kinetics of the enantioselective oxidation of thioanisole **2a** with 35% H_2O_2 (1.2 equiv) catalyzed by [Fe(acac)$_3$] (2 mol%), Schiff base (*S*)-**1a** (4 mol%) and **AH7** (1 mol%). The NMR conversion of **2a** (×) into sulfoxide **3a** (■) and sulfone **4a** (▲) and the *ee* of **3a** (○) are represented according to time.

a deeper insight into the features of the iron-catalyzed sulfoxidation, and in order to understand the role of the additive, we investigated the impact of the *ee* of the ligand [here (*S*)-**1a**] on the enantioselectivity in the formation of the sulfoxide, with and without **AH7** (Figure 4).

In both cases, a positive nonlinear effect was found. Whereas the NLE was less pronounced without additive, it was more significant when the reaction was performed in the presence of **AH7**. At the present stage the observed asymmetric amplification is difficult to interpret, but it clear-

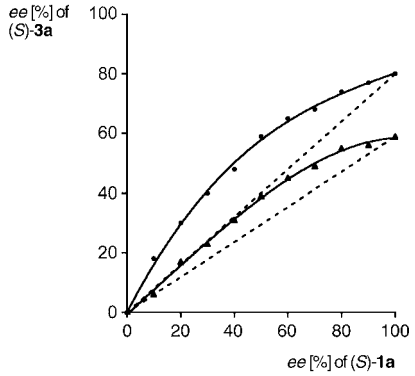


Figure 4. Dependence of the enantioselectivity in the oxidation of **2a** to give **3a** with 35% aq. H_2O_2 catalyzed by $[Fe(acac)_3]$ and (*S*)-**1a** on the *ee* of the ligand, in the absence (▲) and in the presence of **AH7** (●). For comparison, the broken lines indicate a possible linear relationship.

ly indicates that more than one ligand is involved in the stereochemistry-determining step of the catalytic process.

From the great interest in functional enzyme models, which mimic non-heme metalloproteins, especially methane monooxygenase (MMO), a large number of complexes with a (μ-oxo)(μ-carboxylato)diiron core have emerged.[21] Some of them have been demonstrated to be capable of oxidizing substrates with various terminal oxidants.[13,22] In the light of these reports and taking into account that in the sulfide oxidation described here, the best results were obtained with half an equivalent of carboxylic acid (and/or carboxylate salt) relative to iron, and that a positive NLE was observed, it can be suggested that in the reaction medium containing $[Fe(acac)_3]$, the ligand (**1a**) and ArCOOX, a monocarboxylate-bridged diiron(III) complex is generated, which resembles a key intermediate in the catalytic cycle of the oxidative process. Isolation and characterization of such complex, and/or in situ studies are now required to confirm this hypothesis. Until now, however, all attempts to isolate relevant intermediates of such kind remained unsuccessful.[23]

Conclusion

Highly enantioselective oxidations of prochiral sulfides giving synthetically valuable sulfoxides can be performed under simple reaction conditions using a readily available in situ iron catalyst (≤4 mol%) and aqueous hydrogen peroxide. In the presence of small quantities of a carboxylic acid or a carboxylate salt (1 mol%), optically active sulfoxides with excellent enantioselectivities (up to 96% *ee*) are obtained in moderate to good yields (up to 78%). The simplicity of the reaction protocol (aerobic conditions at ambient temperature) and the high *ee* values of the products render this process attractive and make it an interesting alternative to the existing methodology. Our studies reveal that the enantioselectivity directly originates for the asymmetric sulfide oxidation and that the overoxidation to the corresponding sulfones has almost no influence on the *ee* of the product. An asymmetric amplification was observed, which is in accord with our previous hypothesis of the presence of a possible catalytically active species containing two chiral ligands. We are currently trying to isolate and characterize such intermediates and explore further improvements of the experimental conditions.

Experimental Section

General methods: ^1H and ^{13}C NMR spectra were obtained on a Varian Gemini 300 or Innova 400 spectrometer. In all measurements $CDCl_3$ was used as solvent. Chemical shifts δ are given in ppm relative to TMS as internal standard. Optical rotations were measured on a Perkin–Elmer PE-241 apparatus. The enantiomer ratios of sulfoxides **3** were determined by chiral HPLC (Gynkotek apparatus; UV detector UVD 170S (λ 254 nm); 20°C).[24] Absolute configurations were assigned by comparison of the sign of the specific rotations with literature data. When it was necessary, samples of racemic sulfoxides were prepared, according to the literature.[25] All the reactions were performed at room temperature under air.

Materials: All chemicals were used as provided without further purification. Iron(III) acetylacetonate was purchased from Aldrich, 35% aqueous hydrogen peroxide from Acros, and 3,5-diiodosalicylaldehyde from Lancaster. (*S*)- and (*R*)-*tert*-Leucine were provided by Degussa and reduced to *tert*-leucinol according to the literature.[26]

Monitoring of the reactions: The conversion of phenyl methyl sulfide (thioanisole) (**2a**) to phenyl methyl sulfoxide (**3a**) and phenyl methyl sulfone (**4a**) was measured by integration of the methyl group signals in the ^1H NMR spectra of the corresponding compounds on the crude product mixture: Ph-S-*Me*, 2.5 ppm; Ph-S(O)-*Me*, 2.7 ppm; Ph-S(O_2)-*Me*, 3.1 ppm.

(*S*)-(−)-2-(*N*-3,5-Diiodosalicyliden)amino-3,3-dimethyl-1-butanol (1a):[9d] A solution of (*S*)-*tert*-leucinol (313 mg, 2.7 mmol) in ethanol (2 mL) was added to a suspension of 3,5-diiodosalicylaldehyde (1 g, 2.7 mmol) in ethanol (4 mL), and the resulting deep-yellow mixture was kept under stirring. After 16 h, the solvent was evaporated, and the residue was recrystallized in cyclohexane to afford **1a** as yellow needles (65–75% yield). M.p. 163–164°C; $[\alpha]_D = -16.6$ ($c = 1.0$ in acetone); ^1H NMR: $\delta = 0.93$ (s, 9H), 3.01 (dd, $J = 9.6$, 2.9 Hz, 1H), 3.62 (dd, $J = 11.4$, 9.7 Hz, 1H), 3.94 (dd, $J = 11.3$, 2.4 Hz, 1H), 4.40 (brs, 1H), 7.45 (d, $J = 2.2$ Hz, 1H), 7.96 (d, J = 2.0 Hz, 1H), 8.02 (s, 1H), 14.59 (brs, 1H); ^{13}C NMR: $\delta = 26.8$, 32.9, 61.8, 75.6, 77.9, 93.2, 116.7, 141.2, 150.0, 164.7, 167.2.

General procedure for asymmetric oxidation of sulfides: $[Fe(acac)_3]$ (7.1 mg, 0.02 mmol) and Schiff base (*S*)-**1a** (18.9 mg, 0.04 mmol) were dissolved in dichloromethane (0.7 mL), and the clear red solution was stirred until it turned clear brown (15 min). This solution was then added to a suspension of 4-methoxybenzoic acid **AH7** (1.5 mg, 0.01 mmol) [or of the corresponding lithium salt **ALi7** (1.6 mg, 0.01 mmol) in dichloromethane (0.5 mL) in a 10 mL flask, and the resulting mixture was stirred for 10 min. A solution of sulfide **2** (1 mmol) in dichloromethane (0.8 mL) was then added to the previous solution, followed by the dropwise addition of aqueous H_2O_2 (35%; 1.2 mmol). The flask was capped, and the reaction mixture was slowly stirred at room temperature (approximately 150 rpm). After 16 h, the aqueous layer was separated, and the organic layer was dried over $MgSO_4$, filtered, and the solvent was removed in vacuo. The product was then purified by flash chromatography on silica gel (pentane/diethyl ether 1:2, then ethyl acetate).

(*S*)-(−)-Phenyl methyl sulfoxide (3a): Reaction was performed with **ALi7**. Purification by silica gel chromatography afforded the product as a colorless oil (88 mg, 63%, 90% *ee*). $[\alpha]_D = -130.1$ ($c = 1.7$ in acetone); lit: $[\alpha]_D = +130$ ($c = 1.7$ in acetone) for (*R*), 89% *ee*;[27] ^1H NMR: $\delta = 2.72$ (s, 3H), 7.52 (m, 3H), 7.65 (m, 2H); HPLC: t_r (*R*) = 26.5 min, t_r (*S*) = 31.2 min (Chiralcel OD; flow rate, 0.5 mL min^{-1}; heptane/*i*PrOH 9:1).

(*S*)-(−)-Phenyl ethyl sulfoxide (3b): Reaction was performed with **ALi7**. Purification by silica gel chromatography afforded the product as a colorless oil (87 mg, 56%, 82% *ee*). $[\alpha]_D = -169.1$ ($c = 1.4$ in EtOH); lit:

$[\alpha]_D = -143.1$ ($c = 1.4$ in EtOH) for (*S*), 74% *ee*;[28] ^{1}H NMR: $\delta = 1.20$ (t, $J = 7.4$ Hz, 3H), 2.84 (m, 2H), 7.52 (m, 3H), 7.62 (m, 2H); HPLC: t_r (*R*) = 22.0 min, t_r (*S*) = 27.2 min (Chiralcel OD; flow rate, 0.5 mL min^{-1}; heptane/*i*PrOH 9:1).

(*S*)-(−)-Phenyl benzyl sulfoxide (3c): Reaction was performed with **AH7**. Purification by silica gel chromatography afforded the product as a white solid (158 mg, 73%, 79% *ee*). $[\alpha]_D = -169.8$ ($c = 1.0$ in acetone); lit: $[\alpha]_D = -91.0$ ($c = 1.0$ in acetone) for (*S*), 36% *ee*;[29] ^{1}H NMR: $\delta = 4.00$ (d, $J = 12.6$ Hz, 1H), 4.10 (d, $J = 12.6$ Hz, 1H), 6.99 (m, 2H), 7.26 (m, 3H), 7.41 (m, 5H); HPLC: t_r (*R*) = 28.8 min, t_r (*S*) = 36.1 min (Chiralcel OD; flow rate, 0.5 mL min^{-1}; heptane/*i*PrOH 9:1).

(*S*)-(−)-4-Tolyl methyl sulfoxide (3d): Reaction was performed with **ALi7**. Purification by silica gel chromatography afforded the product as a white solid (120 mg, 78%, 92% *ee*). $[\alpha]_D = -126.9$ ($c = 2.0$ in acetone); lit: $[\alpha]_D = +132$ ($c = 2.0$ in acetone) for (*R*), 91% *ee*;[27] ^{1}H NMR: $\delta = 2.42$ (s, 3H), 2.71 (s, 3H), 7.33 (d, $J = 8.0$ Hz, 2H), 7.53 (d, $J = 8.0$ Hz, 2H); HPLC: t_r (*R*) = 24.0 min, t_r (*S*) = 26.2 min (Chiralcel OD; flow rate, 0.5 mL min^{-1}; heptane/*i*PrOH 9:1).

(*S*)-(−)-4-Methoxyphenyl methyl sulfoxide (3e): Reaction was performed with **ALi7**. Purification by silica gel chromatography afforded the product as a pale yellow oil (112 mg, 66%, 86% *ee*). $[\alpha]_D = -129.7$ ($c = 2.0$ in $CHCl_3$); lit: $[\alpha]_D = -102$ ($c = 2.0$ in $CHCl_3$) for (*S*), 86% *ee*;[27] ^{1}H NMR: $\delta = 2.71$ (s, 3H), 3.86 (s, 3H), 7.04 (d, $J = 8.9$ Hz, 2H), 7.60 (d, $J = 8.9$ Hz, 2H); HPLC: t_r (*S*) = 50.0 min, t_r (*R*) = 92.1 min (Chiralcel OB; flow rate, 0.5 mL min^{-1}; heptane/*i*PrOH 7:3).

(*S*)-(−)-4-Bromophenyl methyl sulfoxide (3f): Reaction was performed with **ALi7**. Purification by silica gel chromatography afforded the product as a white solid (130 mg, 59%, 94% *ee*). $[\alpha]_D = -97.5$ ($c = 1.8$ in acetone); lit: $[\alpha]_D = +77$ ($c = 1.8$ in acetone) for (*R*), 80% *ee*;[27] ^{1}H NMR: $\delta = 2.65$ (s, 3H), 7.46 (d, $J = 8.7$ Hz, 2H), 7.61 (d, $J = 8.7$ Hz, 2H); HPLC: t_r (*S*) = 25.8 min, t_r (*R*) = 35.9 min (Chiralcel OB; flow rate, 0.5 mL min^{-1}; heptane/*i*PrOH 8:2).

(*S*)-(−)-4-Chlorophenyl methyl sulfoxide (3g): Reaction was performed with **AH7**. Purification by silica gel chromatography afforded the product as a colorless oil (92 mg, 60%, 92% *ee*). $[\alpha]_D = -109.7$ ($c = 2.0$ in acetone); lit: $[\alpha]_D = +97$ ($c = 2.0$ in acetone) for (*R*), 78% *ee*;[27] ^{1}H NMR: $\delta = 2.73$ (s, 3H), 7.52 (d, $J = 8.6$ Hz, 2H), 7.60 (d, J = 8.6 Hz, 2H); HPLC: t_r (*S*) = 19.9 min, t_r (*R*) = 30.0 min (Chiralcel OB; flow rate, 0.5 mL min^{-1}; heptane/*i*PrOH 8:2)

(*S*)-(−)-4-Nitrophenyl methyl sulfoxide (3h): Reaction was performed with **ALi7**. Purification by silica gel chromatography afforded the product as a white solid (66 mg, 36%, 96% *ee*). $[\alpha]_D = -128.5$ ($c = 0.75$ in $CHCl_3$); lit: $[\alpha]_D = +156.9$ ($c = 0.75$ in $CHCl_3$) for (*R*), 99.3% *ee*;[30] ^{1}H NMR: $\delta = 2.80$ (s, 3H), 7.85, (d, $J = 8.9$ Hz, 2H), 8.40 (d, $J = 8.9$ Hz, 2H); HPLC: t_r (*R*) = 42.9 min, t_r (*S*) = 47.5 min (Chiralcel OJ; flow rate, 0.5 mL min^{-1}; heptane/*i*PrOH 7:3).

(−)-2-Bromophenyl methyl sulfoxide (3i): Reaction was performed with **ALi7**. Purification by silica gel chromatography afforded the product as a yellow oil (105 mg, 48%, 66% *ee*). $[\alpha]_D = -174.9$ ($c = 1.3$ in $CHCl_3$); ^{1}H NMR: $\delta = 2.83$ (s, 3H), 7.38 (m, 1H), 7.59 (m, 2H), 7.95 (m, 1H); HPLC: t_r (−) = 19.3 min, t_r (+) = 28.9 min (Chiralcel OB; flow rate, 0.5 mL min^{-1}; heptane/*i*PrOH 8:2).

(*S*)-(−)-2-Methoxyphenyl methyl sulfoxide (3j): Reaction was performed with **ALi7**. Purification by silica gel chromatography afforded the product as a yellow oil (85 mg, 50%, 70% *ee*). $[\alpha]_D = -36.0$ ($c = 0.9$ in acetone); lit: $[\alpha]_D = +318.6$ ($c = 1.0$ in acetone) for (*R*), 98% *ee*;[31] ^{1}H NMR: $\delta = 2.79$ (s, 3H), 3.89 (s, 3H), 6.94 (d, $J = 8.3$ Hz, 1H), 7.20 (d, $J = 7.5$ Hz, 1H), 7.46 (m, 1H), 7.82 (m, 1H); HPLC: t_r (*S*) = 19.1 min, t_r (*R*) = 36.15 min (Chiralcel OB; flow rate, 0.5 mL min^{-1}; heptane/*i*PrOH 8:2).

(*S*)-(−)-Mesityl methyl sulfoxide (3k): Reaction was performed with **ALi7**. Purification by silica gel chromatography afforded the product as a yellow oil (80 mg, 44%, 77% *ee*). $[\alpha]_D = -180$ ($c = 0.9$ in acetone); lit: $[\alpha]_D = -241$ ($c = 1.0$ in acetone) for (*S*), 98% *ee*;[32] ^{1}H NMR: $\delta = 2.29$ (s, 3H), 2.55 (s, 6H), 2.89 (s, 3H), 6.88 (s, 2H); HPLC: t_r (*R*) = 17.3 min, t_r (*S*) = 26.9 min (Chiralcel OD; flow rate, 0.5 mL min^{-1}; heptane/*i*PrOH 9:1).

(*S*)-(−)-2-Naphthyl methyl sulfoxide (3l): Reaction was performed with **AH7**. Purification by silica gel chromatography afforded the product as a white solid (127 mg, 67%, 95% *ee*). $[\alpha]_D = -133.1$ ($c = 2.0$ in $CHCl_3$); lit: $[\alpha]_D = +127$ ($c = 2.0$ in $CHCl_3$) for (*R*), 90% *ee*;[30] ^{1}H NMR: $\delta = 2.80$ (s, 3H), 7.60 (m, 3H), 7.93 (m, 2H), 7.99 (d, $J = 8.8$ Hz, 1H), 8.22 (s, 1H); HPLC: t_r (*R*) = 37.2 min, t_r (*S*) = 40.8 min (Chiralcel OD; flow rate, 0.5 mL min^{-1}; heptane/*i*PrOH 9:1).

(*S*)-(−)-Phenyl vinyl sulfoxide (3m): Reaction was performed with **ALi7**. Purification by silica gel chromatography afforded the product as a yellow oil (52 mg, 34%, 75% *ee*). $[\alpha]_D = -160$ ($c = 0.5$ in acetone); lit: $[\alpha]_D = -120$ ($c = 1.0$ in acetone) for (*S*), 39% *ee*;[29] ^{1}H NMR: $\delta = 5.91$ (d, $J = 9.6$ Hz, 1H), 6.21 (d, $J = 16.1$ Hz, 1H), 6.60 (dd, $J = 9.6$ Hz, $J = 16.4$ Hz, 1H), 7.51 (m, 3H), 7.63 (m, 2H); HPLC: t_r (*S*) = 21.5 min, t_r (*R*) = 31.1 min (Chiralcel OB; flow rate, 0.5 mL min^{-1}; heptane/*i*PrOH 8:2).

(*S*)-(−)-Phenyl allyl sulfoxide (3n): Reaction was performed with **ALi7**. Purification by silica gel chromatography afforded the product as a yellow oil (104 mg, 63%, 71% *ee*). $[\alpha]_D = -143$ ($c = 1.0$ in acetone); lit: $[\alpha]_D = -107$ ($c = 1.0$ in acetone) for (*S*) 61% *ee*;[29] ^{1}H NMR: $\delta = 3.55$ (m, 2H), 5.20 (d, $J = 16.8$ Hz, 1H), 5.34 (d, $J = 10.1$ Hz, 1H), 5.66 (m, 1H), 7.52 (m, 3H), 7.60 (m, 2H); HPLC: t_r (*S*) = 19.6 min, t_r (*R*) = 34.4 min (Chiralcel OB; flow rate, 0.5 mL min^{-1}; heptane/*i*PrOH 8:2).

(+)-Benzyl methyl sulfoxide (3o): Reaction was performed with **ALi7**. Purification by silica gel chromatography afforded the product (99 mg, 64%, 23% *ee*). $[\alpha]_D = +21$ ($c = 1.9$ in EtOH); lit: $[\alpha]_D = -33.6$ ($c = 3.0$ in EtOH), 58% *ee*;[30] ^{1}H NMR: $\delta = 2.47$ (s, 3H), 3.92 (d, $J = 12.8$ Hz, 1H), 4.08 (d, $J = 12.6$ Hz, 1H), 7.35 (m, 5H); HPLC: t_r (+) = 22.8 min, t_r (−) = 28.4 min (Chiralcel OB; flow rate, 0.5 mL min^{-1}; heptane/*i*PrOH 8:2).

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