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Highly enantioselective sulfoxidation with vanadium catalysts of Schiff bases derived from bromo- and iodo-functionalized hydroxynaphthaldehydes

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ABSTRACT

Two series of chiral Schiff bases, **4a**–**e** and **5a**–**e**, prepared from the condensation of the mono-, di-, tribromohydroxynaphthaldehyde or monoiodohydroxynaphthaldehyde with chiral amino alcohols, were used in combination with $VO(acac)_2$ for the asymmetric oxidation of aryl methyl sulfides using H_2O_2 as terminal oxidant. Among these Schiff bases, dibromo-functionalized **4d** and iodo-functionalized **5e** gave high yields (91–93%) with good enantioselectivities (80–82% ee) for the oxidation of thioanisole in dichloromethane. The asymmetric oxidation of thioanisole *in toluene* using these Schiff bases gave methyl phenyl sulfoxide in satisfactory isolated yields (48–62%) with high enantioselectivities (91–94% ee), which were further improved by a modified procedure with the ee value up to 98% in 62% yield. The oxidations of other aryl methyl sulfides *in toluene* with dibromo- and iodo-functionalized Schiff bases **5d** and **5e** as ligands using the modified procedure afforded the corresponding sulfoxides in 55–67% isolated yields with 95–99% ee.

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1. Introduction

Asymmetric oxidation of prochiral sulfides has attracted extensive attention for decades as enantiopure sulfoxides are important chiral auxiliaries and synthons used in asymmetric synthesis [1–4]. The special biological property of the chiral drugs containing a sulfinyl group with a defined configuration is another reason for the current interest in efficient synthesis of enantiopure sulfoxides [5–8]. Since the pioneer work on the asymmetric oxidation of sulfides using $Ti(O\text{-}i\text{-}Pr)_4$/chiral tartrate systems was reported by Kagan, Modena and their co-workers [9,10], asymmetric oxidations of prochiral sulfides catalyzed by chiral transition metal complexes [1–4,11–14] or chiral organic compounds [15–22] have been extensively investigated.

In the past decades, Bolm's catalysts, namely, $VO(acac)_2$/ and $Fe(acac)_3$/Schiff base systems [12,23–25] have received considerable attention. The advantages of this catalyst system include good-to-high activity and enantioselectivity, the convenient preparation and easy modification of chiral Schiff base ligands, the utilization of cheap and environmentally benign terminal oxidant (H_2O_2), and the facile reaction conditions and easy workup. Investigations on this catalyst system have mainly focused on structural modification of chiral Schiff bases, especially the substituents in the salicylidenyl moiety of the Schiff base, to enhance the enantioselectivity of the reaction. Different substituents, such as *tert*-butyl [23,26], nitro [23,27], aryl [28], bromo [29], iodo [30–32], and even the substituent with an additional chiral element [32–35], have been introduced to the amino alcohol moiety and the 3- and/or 5-position of the salicylidenyl moiety of the Schiff base, and their influences on the asymmetric oxidation of sulfides have been reported. It was found that the vanadium-based catalysts of 3,5-dibromo- and 3,5-diiodo-functionalized chiral Schiff bases displayed considerably improved enantioselectivity in the asymmetric oxidation of sulfides when compared to other analogous Schiff bases [29–32]. For example, the oxidation of thioanisole in dichloromethane at 0 °C with 3,5-diiodo (*S*)-**1** as ligand (Fig. 1) in a PhSMe:$VO(acac)_2$:ligand:-H_2O_2 molar ratio of 100:1:1.5:120 gave 90% ee and 81% yield of methyl phenyl sulfoxide [32], and with 3,5-diiodo (*R*)-**1** as ligand (Fig. 1) in chloroform at 0 °C, the enantioselectivity of the reaction is up to 96.7% ee with 70% yield [30]. The ligand (*R*,*S*)-**3** containing an axially chiral binaphthyl or biphenyl moiety (Fig. 1) in combination with $VO(acac)_2$ afforded the enantioselectivity up to 86% ee with 90% yield for the oxidation of thioanisole in dichloromethane at 0 °C [34]. However, for all reported $VO(acac)_2$/ and $Fe(acac)_3$/Schiff base catalyst systems, the high enantioselectivity could be obtained only when the oxidation of

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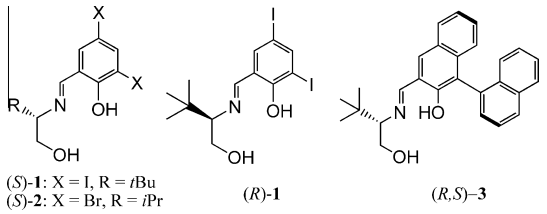


Fig. 1. Structures of some effective chiral Schiff bases for Bolm's catalyst system.

sulfides was carried out in dichloromethane or chloroform at 0 °C [23–37]. This limit of applicable solvents to toxic small haloalkanes makes the vanadium-based catalyst systems less environmental benign and decreases their industrial application value. Therefore, it is necessary to explore new high-performance chiral Schiff bases that, in combination with $VO(acac)_2$, can catalyze the asymmetric oxidation of sulfides in a less-toxic solvent to afford chiral sulfoxides with high enantioselectivity and yields.

We recently prepared two series of chiral Schiff bases, **4a**–**e** and **5a**–**e** (Fig. 2), from the condensation reactions of mono-, di-, tribromohydroxynaphthaldehyde or monoiodohydroxynaphthaldehyde with chiral amino alcohols, either (*S*)-valinol or (*S*)-*tert*-leucinol [38]. There is only one report on the catalytic behavior of the vanadium-based catalyst in combination with the halohydroxynaphthaldehyde-derived Schiff base (**5g**, Fig. 2) for the oxidation of ethyl phenyl sulfide and methyl 2-naphthyl sulfide [32]. We screened the catalytic behaviors of **4a**–**e** and **5a**–**e** in combination with $VO(acac)_2$ for the asymmetric oxidation of prochiral sulfides using H_2O_2 as terminal oxidant in dichloromethane and toluene. The catalytic performances of the reference Schiff bases **4f** and **5f** without halo substituent was also explored to see the effect of the halo group of the ligand on the asymmetric sulfoxidation by comparison. High-to-excellent enantioselectivities with satisfactory yields of sulfoxides were achieved for the asymmetric oxidations of aryl methyl sulfides *in toluene* with vanadium catalysts of the Schiff bases derived from bromo- and iodo-functionalized hydroxynaphthaldehydes.

2. Experimental

2.1. Materials and methods

Compound $VO(acac)_2$ was purchased from Alfa Aesar. All aryl methyl sulfides were purchased from Aldrich and chiral amino acids (*S*)-*tert*-leucine and (*S*)-valine from Aldrich and GL Biochem (Shanghai) Ltd., respectively. 2-Naphthol, 1-naphthaldehyde, and other starting compounds of reagent grade were obtained from local suppliers and used as received. Schiff bases **4f** and **5f** were prepared according to literature procedures [39–41]. The others, **4a–e** and **5a–e**, are new Schiff bases and their preparation and characterization will be described elsewhere [38].

Conversions of sulfides were obtained by GC analysis using HP 5 column with chlorobenzene as internal standard. Enantiomeric excesses (ee) of sulfoxides were determined by HPLC analysis using chiral columns (Daicel Chiracel OD-H, 25 cm × 0.46 cm i.d. and Daicel Chiracel OB-H, 25 cm × 0.46 cm i.d.).

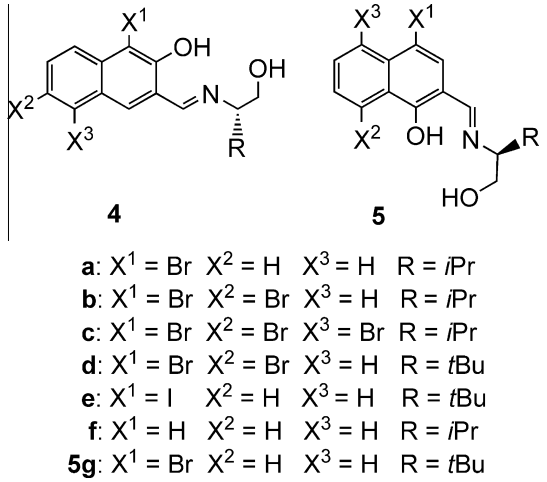


Fig. 2. The chiral Schiff bases used in the present work.

2.2. A general procedure for the asymmetric oxidation of thioanisole

Compound $VO(acac)_2$ (2.7 mg, 0.01 mmol) and a Schiff base ligand (0.015 mmol) were dissolved in solvent (1 mL). The mixture was stirred at room temperature until it turned brown (ca. 30 min). A solution of the sulfide (1.0 mmol) in solvent (1.0 mL) was then added, followed by dropwise addition (ca. 30 min) of aqueous H_2O_2 (30%, 1.2 mmol) at 0 °C. After the mixture was stirred at 0 °C for a certain time, the resulting solution was extracted with dichloromethane. The organic layer was washed with brine and dried over Na_2SO_4. Filtration and evaporation gave a residue, which was purified by flash chromatography on silica gel with petroleum ether/ethyl acetate (3:2, *V*/*V*) and then ethyl acetate as eluents. The pure sulfoxide was obtained after removal of the solvent by rotary evaporation. The enantiomeric excess of the sulfoxide was determined by HPLC analysis.

2.3. A modified procedure for asymmetric oxidation of aryl methyl sulfides in toluene

The toluene solution (1 mL) of $VO(acac)_2$ (2.7 mg, 0.01 mmol) and a Schiff base ligand (0.015 mmol) was stirred at room temperature until it turned brown (ca. 30 min). A solution of the sulfide (1.0 mmol) in toluene (1.0 mL) was then added, followed by dropwise addition (ca. 30 min) of aqueous H_2O_2 (30%, 1.2 mmol) at 0 °C. The mixture was stirred at 0 °C for ca. 4 h. When the reaction reached its equilibrium (monitored by GC analysis), the additional aqueous H_2O_2 (30%, 0.3 mmol) was dropwise added at 0 °C and the solution was stirred for another 4 h. The following workup was identical with the general procedure described in Section 2.2.

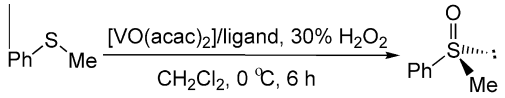
3. Results and discussion

3.1. Influences of Schiff bases *4a–f* and *5a–f* on the asymmetric oxidation of thioanisole

In initial studies, the influence of the structures of the Schiff bases, **4a–f** and **5a–f**, on the activity and enantioselectivity was studied using thioanisole as a probe substrate. Considering the optimal conditions previously reported for the $VO(acac)_2$/Schiff base catalyst systems [28,32,34], the reactions were carried out in a molar ratio of 100:1:1.5:120 for sulfide:$VO(acac)_2$:ligand:H_2O_2 in dichloromethane at 0 °C for a direct comparison of the catalytic results obtained from the present work to those reported for analogous vanadium-based catalysts. The catalytic results are given in Table 1. Each catalytic reaction was repeated at least two times.

The control experiment for the oxidation of thioanisole was carried out with 1% mol of $VO(acac)_2$ and 1.2 equiv of H_2O_2 in the absence of Schiff base ligand in CH_2Cl_2 at 0 °C for 6 h, methyl phenyl sulfoxide was obtained in a high yield (>80%) [42]. With $VO(acac)_2$/**4a** as catalyst system, the reaction was close to end in 4 h under the same conditions, monitored by the on-line GC analysis (Fig. S1), and the HPLC analysis shows that the enantioselectivity

Table 1
Effect of chiral Schiff base ligands on the vanadium-catalyzed asymmetric oxidation of thioanisole with H_2O_2 as terminal oxidant in dichloromethane at 0 °C.[a]



Entry	Ligand	Halo group	*R*	Yield[b] (%)	ee[c,d] (%)
1	**4a**	1-Br	*i*Pr	93	76
2	**4b**	1,6-Br_2	*i*Pr	91	80
3	**4c**	1,5,6-Br_3	*i*Pr	89	71
4	**4d**	1,6-Br_2	*t*Bu	**93**	**82**
5	**4e**	1-I	*t*Bu	91	75
6	**4f**	No halo group	*i*Pr	84	67
7	**5a**	1-Br	*i*Pr	79	67
8	**5b**	1,5-Br_2	*i*Pr	81	78
9	**5c**	1,5,8-Br_3	*i*Pr	91	70
10	**5d**	1,5-Br_2	*t*Bu	84	79
11	**5e**	1-I	*t*Bu	**91**	**80**
12	**5f**	No halo group	*i*Pr	85	60
13	(*S*)-**1**	3,5-I_2	*t*Bu	80 (81)	87 (90)[e]
14	(*R*,*S*)-**3**	Axially chiral 1,1-binaphthyl	*t*Bu	92	78[f]

[a] Reaction conditions: $VO(acac)_2$ (0.01 mmol), ligand (0.015 mmol), thioanisole (1.0 mmol), aqueous H_2O_2 (30%, 1.2 mmol), 0 °C, 6 h, CH_2Cl_2 (2 mL).
[b] Isolated yield.
[c] Determined by HPLC with Daicel Chiralcel OD-H column *V*(hexane)/*V*(*i*-PrOH) = 9:1.
[d] The absolute configuration was assigned by comparing optical rotations and HPLC elution orders with literature data. All of the major enantiomers are in the *S* configuration.
[e] Data cited from Ref. [31]. The data in the brackets were obtained by using 27% H_2O_2 [32].
[f] Data cited from Ref. [33].

almost remains constant during the reaction (6 h) [25], with the ee values of 70–76%. Entries 1–3 and 6 for **4a**–**c** and **4f**, respectively, show that the enantioselectivities are considerably improved by introduction of one or two bromo groups to the naphthyl ring. Schiff base **4b** with two bromine atoms at the 1,6-positions of the naphthyl ring gives a better enantioselectivity (80% ee) when compared to **4a** with one bromine atom at 1-position and **4c** with three bromine atoms at the 1,5,6-positions (entry 2 vs. entries 1 and 3). The order of the enantioselectivities obtained is **4b** > **4a** > **4c** > **4f**. Introduction of the first bromine atom to the para-position of the naphthol OH group of **5f** also display a positive effect on the enantioselectivity of the sulfoxide (entry 7 vs. 12). The secondly introduced bromine atom, being close to the naphthol OH group ready for chelating the vanadium unit, results in apparent improvement of the enantioselectivity (entry 8 vs. entries 7 and 12), while introduction of the third bromine atom to the naphthyl ring results in decrease of the enantioselectivity (entry 9 vs. 8) in a similar trend observed in the **4a**–**c** set. Presumably, the electron-withdrawing effect of the multi-bromine atoms abates the coordination ability of the ligand, leading to an easier disassociation of the Schiff base ligand from the vanadium centre. The catalyst of $VO(acac)_2$/iodo-functionalized Schiff base **5e** gives methyl phenyl sulfoxide in 91% yield and 80% ee (entry 11). These results indicate that both the position and the number of the bromo or iodo substituent in the naphthyl ring of the Schiff base ligand can apparently influence the enantioselectivity. When the R group in the amino alcohol moiety of **4b** is changed from *i*Pr to *t*Bu, the enantioselectivity is slightly increased to 82% ee with 93% yield of sulfoxide (entry 2 vs. 4).

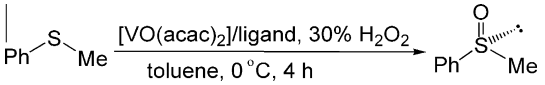
In general, the results given in Table 1 show that the Schiff bases **4a–e** and **5a–e** derived from bromo- and iodo-functionalized hydroxynaphthaldehydes and amino alcohols are good chiral inducers for the asymmetric thioanisole oxidation, to give good-to-high yields (79–93%) of chiral methyl phenyl sulfoxide with moderate-to-good enantioselectivities (67–82% ee). Such a high yield of methyl phenyl sulfoxide indicates that under the condition adopted, only a small amount of the corresponding sulfone is formed, which is supported by the GC analysis of the resulting solution. It is consistent with the previous reports that the good enantioselectivity is a direct result of the asymmetric oxidation of thioanisole in CH_2Cl_2 at 0 °C instead of a kinetic resolution by overoxidation of the initially formed sulfoxide [30,32]. Considering the two aspects of the yield and the enantioselectivity, the result obtained from $VO(acac)_2$/**4d** system (82% ee and 93% yield) is comparable to the best results reported so far for the asymmetric oxidation of thioanisole catalyzed by $VO(acac)_2$ in combination with the Schiff base (*R*,*S*)-**3** (78% ee and 92% yield) [33] and with the diiodo-functionalized Schiff base (*S*)-**1** (87% ee and 80% yield) under similar conditions [31].

3.2. Asymmetric oxidation of thioanisole in toluene

In all reported cases for asymmetric oxidation catalyzed by $VO(acac)_2$/ and $Fe(acac)_3$/Schiff base systems with H_2O_2 as terminal oxidant, dichloromethane and chloroform proved to be optimum solvents [23–37]. In addition to our previous paper [28], only one report describing the asymmetric oxidation of prochiral sulfides and kinetic resolution of racemic sulfoxides in toluene was found in the literature [43]. Using (*R*)-**1** as ligand and with H_2O_2 as terminal oxidant in toluene at 0 °C, the oxidation of thioanisole gave methyl phenyl sulfoxide with modest enantioselectivity (53% ee in toluene cf. 97% ee in chloroform). As toluene is preferred to small haloalkane solvents for reactions on an industrial scale [44], we screened the activity and enantioselectivity of $VO(acac)_2$/**4a–e** and **5a–e** catalyst systems for the asymmetric oxidation of thioanisole in a molar ratio of 100:1:1.5:120 for sulfide:$VO(acac)_2$:ligand:H_2O_2 in toluene at 0 °C. The results are given in Table 2. The influences of other common organic solvents were also studied with **4a** as ligand. We found that solvents have an apparent effect on the enantioselectivity and the yield of asymmetric sulfoxidation reactions. The oxidation of thioanisole in THF, acetonitrile, acetone, ethyl acetate, and chloroform gave low-to-moderate enantioselectivities (14–64% ee and 61–96% yields).

To our delight, the oxidation of thioanisole in toluene gave significantly higher enantioselectivities (91–94% ee) when compared

Table 2
Vanadium-catalyzed asymmetric oxidation of thioanisole with H_2O_2 as terminal oxidant in toluene at 0 °C.[a]



Entry	Ligand	Yield[b] (%)	ee[c,d] (%)
15	**4a**	54	91
16	**4b**	53	92
17	**4d**	48	92
18	**4f**	39	44
19	**5a**	61	91
20	**5b**	61	92
21	**5d**	57	94
22	**5e**	62	93
23	**5f**	63	69
24	(*S*)-**2**	33	87
25	(*R*)-**1**	Not reported	53[e]

[a] Reaction conditions: $VO(acac)_2$ (0.01 mmol), ligand (0.015 mmol), thioanisole (1.0 mmol), aqueous H_2O_2 (30%, 1.2 mmol), 0 °C, 4 h, toluene (2 mL).
[b] See footnotes in Table 1.
[c] See footnotes in Table 1.
[d] See footnotes in Table 1.
[e] Data cited from Ref. [43].

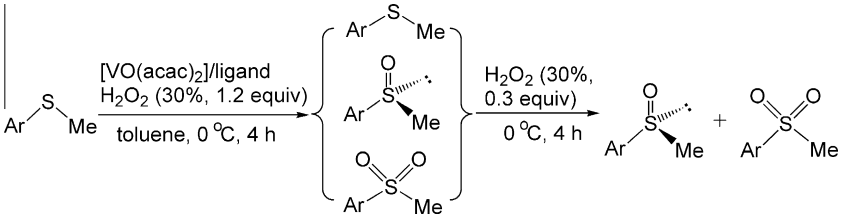
to the results (67–82% ee, Table 1) obtained from the same reaction in dichloromethane under the same condition. In contrast, using Schiff bases **4f** and **5f** without halo substituent as ligands, the enantioselectivities are drastically decreased to 44% ee and 69% ee, respectively (entry 18 vs. entries 15–17 and entry 23 vs. entries 19–22). The results show that the stereoelectronic effect of the bromo and iodo group in the naphthyl moiety of Schiff bases significantly influences the enantioselectivity of the sulfoxidation. The similar effect of the bromo and iodo substituent has been discovered for Schiff bases derived from salicylaldehyde [29–32]. When the Schiff bases **5b** and **5e** containing a dibromo- and iodo-functionalized hydroxynaphthol moiety were used as chiral inducers (entries 20 and 22), the oxidation of thioanisole affords methyl phenyl sulfoxide with high enantioselectivities (92–93% ee) and satisfactory yields (61–62%). In contrast, with the corresponding Schiff bases (*S*)-**2** and (*R*)-**1** (Fig. 1) containing a dibromo- and diiodo-functionalized hydroxyphenyl moiety as ligands (entries 24 and 25), the oxidation of thioanisole gave methyl phenyl sulfoxide with modest-to-good enantioselectivities (87% ee for (*S*)-**2** and 53% ee for (*R*)-**1**) and a low yield (33% for (*S*)-**2**). A comparison of the catalytic results obtained with **5b**, **5e**, (*S*)-**2**, and (*R*)-**1** indicates that the enantioselectivity and activity of the vanadium-based catalysts for the oxidation of thioanisole in toluene can be considerably improved by adjusting the structure of the Schiff base with a bromo- and iodo-functionalized hydroxynaphthylmethyl unit in place of the corresponding salicyl moiety.

3.3. A modified procedure for the enantioselective preparation of aryl methyl sulfoxides in toluene

The GC monitoring of the thioanisole oxidation shows that the reaction in toluene levels off after 3 h (Fig. S2). Although about 20% of thioanisole is left in the solution, the conversion could not be further improved by extending the reaction time or using the mixture of CH_2Cl_2 and toluene as solvent. The GC analysis of the resulting solution indicates that initially formed sulfoxide can be overoxidized to sulfone in toluene even at 0 °C. Only slight enantioselectivity (selectivity factor $S \approx 3$) was observed for the kinetic resolution of racemic methyl phenyl sulfoxide in toluene at 0 °C using **4a** or **5b** as ligand in a molar ratio of 100:1:1.5:80 for sulfoxide:$VO(acac)_2$:ligand:H_2O_2. These results are consistent with the previous report on the low enantioselectivity for oxidation of racemic methyl phenyl sulfoxide in toluene with $VO(acac)_2$/(*R*)-**1** as catalyst and H_2O_2 as terminal oxidant [43]. Therefore, we can conclude that the high enantioselectivities, listed in Table 2, obtained from the oxidation of thioanisole in toluene dominantly result from the asymmetric oxidation of sulfide and the overoxidation of the in-situ generated sulfoxide give only a small contribution to the enantioselectivity of the sulfoxide finally obtained.

To further improve the enantioselectivity of sulfide oxidation in toluene, we explored the influences of the loading amount and the added mode of oxidant H_2O_2 on the reaction. The GC analysis shows the resulting solution, from the oxidation of thioanisole with $VO(acac)_2$/**5b**, /**5d**, and /**5e** as catalysts using 1.2 equiv of H_2O_2 (added at once) in toluene at 0 °C for 4 h, contains the methyl phenyl sulfoxide, sulfone, and unreacted thioanisole with an approximate ratio of 5:3:2. The fact that some thioanisole left in the resulting solution means that 1.2 equiv of H_2O_2 is not enough for the complete conversion of the starting sulfide because the further oxidation of the in-situ formed sulfoxide inevitably, although slowly, occurs in toluene even at 0 °C. When we raised the loading amount of H_2O_2 from 1.2 to 1.3, 1.4, and 1.5 equiv and added it at once in the beginning of the reaction, both the enantioselectivity and the yield were apparently decreased with increase in the concentration of H_2O_2 [26,42]. Therefore, a modified procedure with addition of H_2O_2 at twice was adopted. A 1.2 equiv of H_2O_2 was dropped at 0 °C in the beginning of the reaction, and after the mixture was stirred for 4 h the additional 0.3 equiv of H_2O_2 was added

Table 3
A modified procedure for vanadium-catalyzed asymmetric oxidation of aryl methyl sulfides with H_2O_2 as terminal oxidant in toluene at 0 °C.[a]



Entry	Ligand	Ar	Yield[b] (%)	ee[c,d] (%)
20[e]	**5b**	Ph	61	92
26	**5b**	Ph	59	97
21[e]	**5d**	Ph	57	94
27	**5d**	Ph	51	95
22[e]	**5e**	Ph	62	93
28	**5e**	Ph	62	98
29	**5d**	4-BrC_6H_4	65	97
30	**5e**	4-BrC_6H_4	58	96
31	**5d**	4-$MeOC_6H_4$	59	95
32	**5e**	4-$MeOC_6H_4$	55	97
33	**5d**	2-Naphthyl	67	98
34	**5e**	2-Naphthyl	61	99

[a] Reaction conditions: $VO(acac)_2$ (0.01 mmol), ligand (0.015 mmol), aryl methyl (1.0 mmol), aqueous H_2O_2 (30%, 1.2 + 0.3 mmol, added by two portions), toluene (2 mL).
[b] Isolated yield.
[c] Determined by HPLC with Daicel Chiralcel OD-H column *V*(hexane)/*V*(*i*-PrOH) = 9:1 for entries 20–22, 26–28, 33 and 34; Daicel Chiralcel OB-H column *V*(hexane)/*V*(*i*-PrOH) = 8:2 for entries 29 and 30, 5:5 for entries 31 and 32.
[d] See the footnote *d* in Table 1.
[e] H_2O_2 (30%, 1.2 mmol, added at once in the beginning of the reaction). The other conditions are the same as that described in the footnote *a*.

to the same reaction vessel. The reaction was extended for another 4 h at 0 °C. It is encouraging that excellent enantioselectivities were obtained by using the modified procedure in toluene. The combination of the asymmetric oxidation of the left sulfide and the slightly kinetic resolution of the in-situ formed sulfoxide in the latter step with an extra 0.3 equiv of H_2O_2 made an improvement of the enantioselectivity, while only a tolerant drop in the yield of methyl phenyl sulfoxide was observed. Compared to the enantioselectivities (92–94% ee) and the yields (57–62% yield) obtained from the oxidation of thioanisole in toluene with addition of 1.2 equiv of H_2O_2 at once, **5b**, **5d** and **5e** display better enantioselectivities (95–98% ee, Fig. S3) in 51–62% yields when the modified procedure was adopted (entries 20–22 vs. 26–28 respectively).

With the modified procedure, we performed the asymmetric oxidation of various aryl methyl sulfides with $VO(acac)_2$/**5d** and / **5e** as catalysts. The catalytic results are given in Table 3. The corresponding sulfoxides were obtained in satisfactory isolated yields (55–65%) with excellent enantioselectivities (95–99% ee, Fig. S4). In general, ligand **5d** gave higher yields of sulfoxides than **5e** for the oxidations of all three tested aryl methyl sulfides, while **5d** and **5e** afforded similar enantioselectivities for the oxidation of each aryl methyl sulfide. To the best of our knowledge, these are the best results reported so far for the asymmetric oxidation of aryl methyl sulfides *in toluene* using vanadium catalysts in combination with chiral Schiff bases, which are comparable to the best results obtained from such asymmetric oxidation reactions in dichloromethane or chloroform [23–25,30,32].

4. Conclusions

In conclusion, the Schiff bases **4a**–**e** and **5a**–**e** containing bromo- and iodo-functionalized hydroxynaphthaldehydes are efficient chiral inducers for the vanadium-catalyzed asymmetric oxidations of various aryl methyl sulfides with H_2O_2 as terminal oxidant. A comparison of the catalytic performances of $VO(acac)_2$/Schiff bases **4a**–**e** and **5a**–**e**, as well as their analogous Schiff bases **4f** and **5f** without halo substituent, in the oxidation of thioanisole indicates that the number and the position of the halogen atom on the naphthyl ring of the Schiff base play significant effects on the enantioselectivity of the sulfoxides. More interestingly, using these Schiff bases in combination with $VO(acac)_2$, the asymmetric oxidation of thioanisole *in toluene* afforded methyl phenyl sulfoxide in reasonable yields (48–62%) with relatively high enantioselectivities (91–94% ee), which are significantly higher than the catalytic results obtained from the same reaction in toluene with Schiff bases (*S*)-**2** and (*R*)-**1** containing a dibromo- or diiodo-functionalized salicyl moiety as ligands. With the modified procedure by adding 1.5 equiv of H_2O_2 in two portions, the enantioselectivity for the oxidation of thioanisole in toluene was further improved up to 98% ee with a satisfactory yield (62%) when iodo-functionalized **5e** was used as ligand. The asymmetric oxidations of other aryl methyl sulfides in toluene with dibromo-functionalized **5d** and iodo-functionalized **5e** as ligands, respectively, afforded the corresponding sulfoxides in satisfactory yields (55–65%) with excellent enantioselectivities (95–99% ee), which are the best results ever reported for such sulfide oxidation reactions *in toluene* using vanadium-based catalysts. These results are valuable for the industrial application of these asymmetric sulfoxidation reactions, since as a solvent toluene is preferred over dichloromethane and chloroform in an environment protection point of view.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jcat.2010.05.013.

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