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Influence of substituents in the salicylaldehyde-derived Schiff bases on vanadium-catalyzed asymmetric oxidation of sulfides

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A series of chiral Schiff bases (L^1–L^5) with different substituents in the salicylidenyl unit were prepared from condensation of 3-aryl-5-*tert*-butylsalicylaldehyde derivatives and optically active amino alcohols. Bromination of 3-phenyl-5-*tert*-butylsalicylaldehyde gave an unexpected product 3-(4-bromophenyl)-5-bromosalicylaldehyde, from which the corresponding Schiff base ligands L^6 and L^7, derived from (*S*)-valinol and (*S*)-*tert*-leucinol, respectively, were prepared. Ligands L^1–L^7 were applied to the vanadium-catalyzed asymmetric oxidation of aryl methyl sulfides. Under the optimal conditions, the oxidation of the thioanisole with H_2O_2 as oxidant in CH_2Cl_2 catalyzed by VO(acac)$_2$-L^1–L^7 gives good yields (74–83%) with moderate enantioselectivity (58–77% ee). Ligand L^7, containing a 4-bromophenyl group on the 3-position and a Br atom on the 5-position of the salicylidenyl moiety, displays an 80–90% ee for vanadium-catalyzed oxidation of methyl 4-bromophenyl sulfide and methyl 2-naphthyl sulfide.

Keywords: 3-arylsalicylaldehyde; asymmetric sulfoxidation; chiral Schiff bases; chiral sulfoxides; vanadium catalyst

Introduction

Enantiopure sulfoxides are effective chiral auxiliaries and synthons in asymmetric synthesis and useful ligands in enantioselective catalysis.[1–3] They also play an important role in bioactive ingredients in the pharmaceutical industry.[4,5] Therefore, asymmetric oxidation of prochiral sulfides is an attractive subject in organic synthesis. In the past two decades, asymmetric oxidation of sulfides has been extensively investigated, either promoted by Ti(O-*i*-Pr)$_4$-chiral tartrates[6,7] and chiral organic compounds such as chiral oxaziridines,[8,9] or catalyzed by transition metal complexes of various chiral ligands, such as iron-porphyrins,[10,11] manganese-salens,[12,13] titanium-BINOL,[14,15] titanium-*C*2-symmetric diols,[16,17] zirconium-trialkanol amines,[18] and vanadium-[19–21] and iron-[22] tridentate Schiff base catalyst systems. Among these catalyst systems for asymmetric sulfoxidation, Bolm's catalysts, that is, VO(acac)$_2$–and Fe(acac)$_3$–Schiff base systems, have received considerable attention in recent years because of three attractive advantages: (1) the simplicity, convenient preparation, and easy modification of chiral Schiff base ligands; (2) the utilization of cheap and environmentally benign terminal oxidant (H_2O_2); and (3) the facile reaction conditions and easy workup.[23]

Since Bolm and co-workers developed the effective catalyst system of VO(acac)$_2$–chiral Schiff base for asymmetric oxidation of sulfides in 1995, investigations on this catalyst system have concentrated on three aspects: (1) structural modification of chiral Schiff bases to enhance the enantioselectivity of the systems;[19–21] (2) preparation of vanadium-based catalysts with polymer-supported chiral Schiff bases to improve the recycling property of the catalysts,[24] and (3) broadening of sulfide substrates including the sulfide intermediates of some medicines to explore the practical applications of the catalyst systems.[5,25] Different substituents, such as *tert*-butyl, nitro, bromo, iodo and even the substituent with an additional chiral element, have been introduced to the 3- and/or 5-position of the salicylidenyl moiety, and their influences on the asymmetric oxidation of sulfides have been reported.[19,23,26] The studies showed that the vanadium-based catalysts of chiral Schiff bases with the substituent possessing an additional chiral element on the 3-position of the salicylidenyl moiety displayed apparently higher activity and enantioselectivity in asymmetric oxidation of sulfides.[20] We systematically studied the influence of the substituents, *ortho* to the phenolic hydroxyl group of a chiral Schiff base ligand, on activity and enantioselectivity of the vanadium-based catalysts for asymmetric oxidation of prochiral sulfides. A series of chiral Schiff bases, 2-(*N*-3-aryl-5-*tert*-butylsalicylidene)aminoalcohols ($\mathbf{L^1}$–$\mathbf{L^5}$) and 2-(*N*-3-aryl-5-bromosalicylidene)aminoalcohols ($\mathbf{L^6}$ and $\mathbf{L^7}$), were prepared. To the best of our knowledge, Schiff base ligands $\mathbf{L^5}$–$\mathbf{L^7}$ have not been previously reported in the

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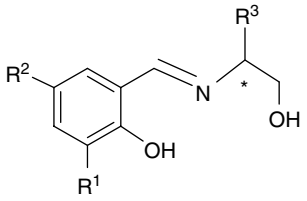


(*S*)-**L**^{1}: $R^1 = C_6H_5$ $R^2 = t$-Bu $R^3 = i$-Pr
(*S*)-**L**^{2}: $R^1 = 4\text{-}CH_3OC_6H_4$ $R^2 = t$-Bu $R^3 = i$-Pr
(*S*)-**L**^{3}: $R^1 = 4\text{-}FC_6H_4$ $R^2 = t$-Bu $R^3 = i$-Pr
(*S*)-**L**^{4}: $R^1 = 1$-naphthyl $R^2 = t$-Bu $R^3 = i$-Pr
(*S*)-**L**^{5}: $R^1 = 1$-naphthyl $R^2 = t$-Bu $R^3 = t$-Bu
(S)-**L**^{6}: $R^1 = 4\text{-}BrC_6H_4$ $R^2 = Br$ $R^3 = i$-Pr
(S)-**L**^{7}: $R^1 = 4\text{-}BrC_6H_4$ $R^2 = Br$ $R^3 = t$-Bu
(*S*)-**L**^{8}: $R^1 = H$ $R^2 = t$-Bu $R^3 = i$-Pr
(*S*)-**L**^{9}: $R^1 = t$-Bu $R^2 = t$-Bu $R^3 = i$-Pr
(*S*)-**L**^{10}: $R^1 = Br$ $R^2 = t$-Bu $R^3 = i$-Pr

Scheme 1.

literature. Asymmetric oxidation of aryl methyl sulfides catalyzed by VO(acac)$_2$–**L**^{1}–**L**^{10} (Scheme 1) was scrutinized with H_2O_2 as terminal oxidant. The influences of solvents, the ratio of VO(acac)$_2$–Schiff base ligand, and the pre-reaction time on the catalytic reaction were first optimized.

Results and Discussion

Synthesis of Schiff base ligands L^{6} and L^{7}

It was reported that the presence of bromine or iodine atoms on the salicylidenyl aromatic ring of a Schiff base ligand could improve the enantioselectivity of the asymmetric oxidation of sulfides.[19,26] To further explore the influence of the halogen atoms on the catalytic reaction, we tried to prepare 5-*tert*-butyl-3-(2,4,6-tribromophenyl)salicylaldehyde by multi-bromination of 5-*tert*-butyl-3-phenylsalicylaldehyde (Scheme 2), which could be readily obtained in high yield by Suzuki–Miyaura coupling reaction of 3-bromo-5-*tert*-butylsalicylaldehyde with phenylboronic acid.[27] Unfortunately, all attempts to attain the designed multi-bromosalicylaldehyde, by enhancing the reaction temperature, extending the reaction time and even using bromine as solvent,[28] failed. The reaction of 5-*tert*-butyl-3-phenylsalicylaldehyde with Br_2 at 50 °C in $CHCl_3$ afforded the 5-bromo-3-(4-bromophenyl)salicylaldehyde in good yield (Scheme 2, 70–75%). Unexpectedly, the *tert*-butyl group of the starting salicylaldehyde is displaced by a bromine atom. The Schiff base ligands **L**^{6} and **L**^{7} were readily prepared in good yields by condensation of an equal amount of 5-bromo-3-(4-bromophenyl)salicylaldehyde and the corresponding chiral amino alcohol.

Optimization of the thioanisole oxidation conditions

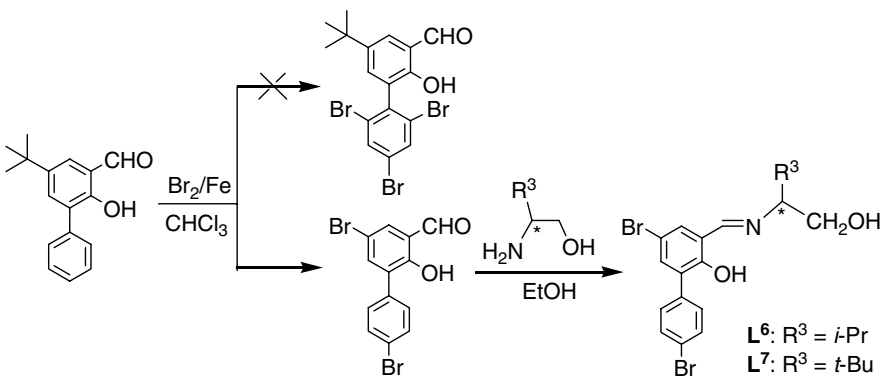
To determine the optimal conditions for the catalytic asymmetric oxidation of aryl methyl sulfides, we used VO(acac)$_2$–Schiff base ligand **L**^{4} as the catalytic system. The influences of catalyst loading amounts, molar ratios of the vanadium compound to the ligand, pre-reaction time and solvents on the reactivity and enantioselectivity of the catalysts were explored using thioanisole as probe substrate with slow addition of aqueous H_2O_2. Tables 1 and 2 give the yields and ee values of the sulfoxide product obtained from the reaction under different conditions.

We first studied the influence of solvents on thioanisole oxidation (entries 1–7). The results show that solvents have an apparent effect on the conversion and the enantioselectivity of

Table 1. Asymmetric oxidation of thioanisole catalyzed by VO(acac)$_2$–**L**^{4} in different solvents[a]

Entry	Solvent	Yield (%)[b]	Ee (%)[c,d]
1	CH_3CN	69	47
2	CCl_4	31	42
3	Toluene	42	46
4	Ethanol	83	39
5	Acetone	91	32
6	$CHCl_3$	66	58
7	CH_2Cl_2	73	57

[a] Reaction conditions: $C_6H_5SCH_3$ (1 mmol), H_2O_2 (30%, 1.15 mmol), VO(acac)$_2$ (0.01 mmol), VO(acac)$_2$–**L**^{4} (1 : 1.5, mol/mol), solvent (2 ml), 0 °C, 8 h, pre-reaction time 60 min.
[b] Isolated yields based on sulfides, and the same for tables 2, 3, and 4.
[c] Determined by HPLC with a Daicel Chiralcel OD-H column, *n*-hexane–*i*-PrOH = 9 : 1 (v/v), and the same below unless stated otherwise.
[d] All reactions give major products of *S*-configuration. Absolute configuration of the major product was determined by comparing its sign of optical rotation with that in Legros and Bolm[29], and the same for tables 2, 3, and 4.



Scheme 2.

Table 2. Asymmetric oxidation of thioanisole catalyzed by $VO(acac)_2$–**L**^{4} under different reaction conditions[a]

Entry	Pre-reaction time (min)	$VO(acac)_2$–**L**^{4} (mol/mol)	$VO(acac)_2$ (mol%)	Yield (%)	Ee (%)
7	60	1 : 1.5	1	73	57
8	60	1 : 2	1	84	57
9	60	1 : 4	1	79	56
10	60	1 : 1.5	0.5	68	57
11	60	1 : 1.5	2	85	58
12	30	1 : 1.5	1	81	59
13	10	1 : 1.5	1	82	61

[a] Reaction conditions: $C_6H_5SCH_3$ (1 mmol), H_2O_2 (30%, 1.15 mmol), CH_2Cl_2 (2 ml), 0 °C, 8 h.

Table 3. Effect of the substituent of the ligand on the asymmetric oxidation of thioanisole[a]

Entry	Ligand	R^1	R^2	R^3	Yield (%)	Ee (%)
14	**L**^{1}	C_6H_5	*t*-Bu	*i*-Pr	74	60
15	**L**^{2}	4-$CH_3OC_6H_4$	*t*-Bu	*i*-Pr	76	59
16	**L**^{3}	4-FC_6H_4	*t*-Bu	*i*-Pr	79	58
17	**L**^{4}	1-Naphthyl	*t*-Bu	*i*-Pr	84	61
18	**L**^{5}	1-Naphthyl	*t*-Bu	*t*-Bu	83	64
19	**L**^{6}	4-BrC_6H_4	Br	*i*-Pr	79	74
20	**L**^{7}	4-BrC_6H_4	Br	*t*-Bu	82	77
21	**L**^{8}	H	*t*-Bu	*i*-Pr	82	52
22	**L**^{9}	*t*-Bu	*t*-Bu	*i*-Pr	80	53
23	**L**^{10}	Br	*t*-Bu	*i*-Pr	79	62

Reaction conditions: $VO(acac)_2$: ligand : $C_6H_5SCH_3$:H_2O_2 = 1 : 2 : 100 : 115, CH_2Cl_2 (2 ml), pre-reaction time 10 min, 0 °C, 8 h.

asymmetric sulfide oxidation reactions. The oxidation in oxygen-containing solvent (CH_3CH_2OH, CH_3COCH_3) gave good yields (83 and 91%) of the sulfoxide but low enantioselectivity (entries 4 and 5), while the reaction in the solvents of weak polarity (CCl_4, $CH_3C_6H_5$) afforded relatively low yields and somewhat improved ee values (entries 2 and 3). Although with $CHCl_3$ as solvent, the ee of the products is almost the same as that with CH_2Cl_2 as solvent under the same reaction conditions (entries 6 and 7), the isolated yield of sulfoxide is lower than that resulting from the reaction in CH_2Cl_2. In general, of all the solvents used, CH_2Cl_2 was found to be the correct solvent for the present catalytic oxidation reaction, which gave a moderate yield (73%, entry 7) and a moderate ee (57%).

As the molar ratio of $VO(acac)_2$: **L**^{4} decreased from 1 : 1.5 to 1 : 2, the yields of the sulfoxide increased from 73 to 84% (entries 7 and 8), while the change of the molar ratio did not influence the ee value. Further decrease in the $VO(acac)_2$: **L**^{4} molar ratio to 1 : 4 did not show considerable influence on either the yield or the ee value (entries 8 and 9). An increase in the loading amount of $VO(acac)_2$ from 0.5 to 2% resulted in a significant improvement in the yield (from 68 to 85%, entries 7, 10 and 11), but the ee values remained unchanged.

When the time for pre-reaction of $VO(acac)_2$ and **L**^{4} in CH_2Cl_2 was shortened from 60 to 10 min, the yield of the sulfoxide was apparently enhanced, and the ee value was slightly increased (entries 7, 12 and 13). Without pre-reaction, that is, instant addition of the substrate to the solution of $VO(acac)_2$ and the ligand gave the similar ee value (60% ee) to that obtained from the reaction with 10–30 min pre-reaction time. The results suggest that the pre-reaction time does not apparently influence the ee values of the reaction, and long-time pre-reaction may cause decomposition of the pre-catalyst.

On the basis of the above results, the catalytic oxidation of aryl methyl sulfides in the following study was carried out using 1 mol% of $VO(acac)_2$ and two equivalents of the ligands relative to $VO(acac)_2$ with 10 min pre-reaction in CH_2Cl_2. According to the literature reports[30,31] and our previous experience,[26] 1.15 equiv of diluted H_2O_2 was slowly dropped into the reaction solution at 0 °C.

Effect of the substituents of the Schiff base ligands on the asymmetric oxidation of thioanisole

Some studies have proved that the electronic and steric effects of the substituents on the 3- and 5-positions of the salicylidenyl moiety in Schiff bases could influence the activity and enantioselectivity of the vanadium catalysts.[19,26] It is convenient to introduce a functionalized aryl group to the 3-position of the salicylidenyl moiety by Suzuki–Miyaura coupling reaction of 3-bromo-5-*tert*-butylsalicylaldehyde and aryl boronic acids, to adjust the performance of vanadium catalysts. Thus, a series of Schiff base ligands **L**^{1}–**L**^{7}, having aryl groups with different electronic and steric effects attached to the 3-position of the salicylidenyl moiety were prepared as chiral ligands for asymmetric oxidation of sulfides. The Schiff base ligands **L**^{8}, **L**^{9} and **L**^{10} with an H atom, a *t*-Bu group or a Br atom on the 3-position of the salicylidenyl unit were also prepared for direct comparison of the catalytic results under the same reaction conditions. The catalytic reactions were carried out with catalyst systems of $VO(acac)_2$–**L**^{1}–**L**^{10} in CH_2Cl_2 using 1.15 equiv of 30% aqueous H_2O_2 as oxidant and thioanisole as substrate. The catalytic results are summarized in Table 3.

The results of entries 14–17 vs 21 show that introduction of an aryl group to the 3-position of the salicylidenyl moiety of the ligand does have a positive effect on the enantioselectivity for thioanisole asymmetric oxidation. The ee values were improved from 52–53% (entries 21 and 22) for R^1 = H and *t*-Bu to 58–61% (entries 14–17) for R^1 = aryl, while they were similar to the value (62% ee) for R = Br. Variation of the electronic and steric effect of the aryl group (R^1) has a trivial influence on the ee value of the product. With the increase in the steric effect of the R^1 group by changing phenyl to 1-naphthyl group, the yields of the sulfoxide were enhanced from 74 to 81%. Replacement of the *i*-Pr group on the chiral carbon of the ligands **L**^{4} and **L**^{6} by the larger *t*-Bu group only slightly increaseed the ee values (entries 17 vs 18, and 19 vs 20). Ligands **L**^{6} and **L**^{7} bearing a 4-BrC_6H_4 group on the 3-position and a Br atom on the 5-position of the salicylidenyl moiety of the ligands showed a higher enantioselectivity than other ligands used. The ligand **L**^{7} derived from (*S*)-*tert*-leucinol afforded the sulfoxide product in 82% yield and 77% ee for the oxidation of thioanisole catalyzed by a vanadium complex (entry 20).

The performance of $VO(acac)_2$–**L**^{7} for catalytic oxidation of different aryl methyl sulfides

From the scrutinizing tests, **L**^{7} emerges as a highly performing ligand for the vanadium-catalysed asymmetric oxidation of

Table 4. Asymmetric oxidation of aryl methyl sulfides using $VO(acac)_2$ – **L**[7] as catalyst[a]

Entry	Ar	Yield (%)	Ee (%)[b]	Config.
20	C_6H_5	82	77	*S*
24	4-$MeOC_6H_4$	77	73	*S*
25	4-BrC_6H_4	76	80	*S*
26	2-Naphthyl	85	90	*S*

[a] The reaction conditions are the same as those in Table 3.
[b] The ee values were determined using HPLC analysis with a Daicel Chiralcel OD-H column and *n*-hexane–*i*-PrOH = 9 : 1 (v/v) for entries 20 and 26, a Daicel Chiralcel OB-H column and *n*-hexane–*i*-PrOH = 5 : 5 (v/v) for entry 24, 8 : 2 for entry 25.

thioanisole. The performance of ligand **L**[7] for vanadium-catalyzed asymmetric oxidation of different aryl methyl sulfide was explored, and the catalytic results are listed in Table 4.

The catalytic oxidations of methyl 4-bromophenyl sulfide and methyl 4-methoxyphenyl sulfide by $VO(acac)_2$–**L**[7] gave similar isolated yields as that for thioanisole. The sulfide with a 4-bromophenyl group afforded higher enantioslelctivity (80% ee) than the sulfide with a 4-methoxyphenyl group (73% ee). As the phenyl group of the sulfide was replaced by a 2-naphthyl group, the yield was increased to 85% with a good enantioselectivity (90% ee).

The catalytic results suggest that introduction of the Br atom to the salicylidenyl unit of Schiff base ligand has a beneficial effect on the enantioselectivity for the vanadium-catalyzed sulfide oxidation. Further investigations are in progress to explore the performance of multi-bromo modified Schiff base ligands and rigid chiral N,O-ligands in the catalytic asymmetric oxidation of sulfides.

Experimental

Materials and instruments

Compound $VO(acac)_2$ and all aryl methyl sulfides were purchased from Alfa Aesar, and chiral amino acids (*S*)-*tert*-leucine and (*S*)-valine from Aldrich and GL Biochem (Shanghai) Ltd., respectively. 3-Bromo-5-*tert*-butylsalicylaldehyde and other starting compounds of reagent grade were obtained from local suppliers and used as received. Chiral amino alcohols were prepared by reduction of corresponding commercially available amino acids as described in the literature.[32] 3-Aryl-substituted salicylaldehyde derivatives, except 3-(4-bromophenyl)-5-bromosalicylaldehyde, were prepared from 3-bromo-5-*tert*-butyl-salicylaldehyde and corresponding aryl boronic acids according to the reported procedures.[27]

The ^1H and ^{13}C NMR spectra were obtained on an Unity Inova 400NMR spectrometer with TMS as internal standard. Mass spectra were performed by electrospray ionization (ESI) on an HP 1100 MSD instrument. Optical rotations at 589 nm were measured with a Jasco P-1010 digital polarimeter. The ee values of sulfoxides were determined by HPLC (Agilent 1100 series) 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.).

Preparation of 3-(4-bromophenyl)-5-bromosalicylaldehyde

A flask was charged with 3-phenyl-5-*tert*-butylsalicylaldehyde (1.27 g, 5.0 mmol), iron dust (20 mg) and 10 ml $CHCl_3$. Bromine (2.61 g, 16.5 mmol) was added dropwise at room temperature. After addition, the mixture was stirred at 50 °C for 24 h. The red solution was then quenched with aqueous $NaHSO_3$ (10%, 30 ml). The layers were separated and the aqueous layer was extracted with dichloromethane (2 × 20 ml). The combined organic layers were washed with brine, dried with anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude residue was chromatographed on a silica gel column using petroleum ether–ethyl acetate (20 : 1, v/v) as eluent. Pure product was obtained as a pale yellow solid (1.26 g, 71%); m.p. 104–106 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 11.74 (s, 1H), 9.89 (s, 1H), 7.69–7.68 (m, 2H), 7.59–7.56 (m, 2H), 7.46–7.43 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 195.7, 157.8, 139.8, 135.1, 133.8, 131.6, 131.6, 130.8, 122.6, 122.0, 111.6. HRMS (ESI): *m/z* calcd for ($C_{13}H_8O_2Br_2$): *m/z* 353.8891, found 353.8886.

General procedure for the preparation of ligands L^1–L^7

An equivalent amount of a chiral amino alcohol and a 3-aryl-substituted salicylaldehyde derivative were dissolved in EtOH. The solution was stirred for 4 h at 60 °C. After the solvent was evaporated under reduced pressure, the residue was subject to flash column chromatography on silica gel using petroleum ether–ethyl acetate as eluent. The filtrate was concentrated until yellow amorphous solids appeared in solution. The desired Schiff base ligands (**L**[1]–**L**[7], Scheme 1) were obtained after the solids were washed with cold ether and dried.

Preparation of Schiff bases **L**[1]–**L**[4] was reported previously.[27] For a comparison of the catalytic results, the (*S*)-2-(*N*-5-*tert*-butylsalicylidene)amino-3-methyl-1-butanol (**L**[8]), (*S*)-2- (*N*-3,5-di-*tert*-butylsalicylidene)amino-3-methyl-1-butanol (**L**[9]) and (*S*)-2-(*N*-3-bromo-5-*tert*-butylsalicylidene)amino-3-methyl-1-butanol (**L**[10]) ligands were prepared following literature protocols.[27,33]

(*S*)-2-[*N*-3-(1-naphthyl)-5-*tert*-butylsalicylidene]-amino-3,3-dimethyl-1-butanol (**L**[5]): yield 74%; m.p.: 83–85 °C. $[\alpha]_{589}^{23} = -111.8°$ (*c* = 0.002, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 13.31 (s br, 1H, O*H*), 8.41 (s, 1H, C*H*=N), 7.82 (t, 1H), 7.67–7.60 (m, 2H), 7.49 (t, 1H), 7.44–7.33 (m, 5H), 3.84–3.58 (m, 2H, CH_2OH), 2.89 (d, 1H, *CH*-N), 1.28 (s, 9H), 0.86 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 166.7 (CH=N), 156.8 ($C_{phenolic}$-OH), 141.2, 136.5, 133.9, 132.5, 132.3, 128.5, 128.3, 128.1, 128.0, 127.8, 126.5, 126.0, 125.8, 125.5, 81.7, 62.7, 34.3, 33.4, 31.7, 27.3. MS (APCI): *m/z* 404.2 $[M + H]^+$.

(*S*)-2-[*N*-3-(4-bromophenyl)-5-bromosalicylidene]amino-3-methyl-1-butanol (**L**[6]): yellow solid, yield 70%; m.p. 52–54 °C. $[\alpha]_{589}^{23} = -19.4°$ (*c* 0.0015, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 14.19 (s, 1H, O*H*), 8.35 (s, 1H, C*H*=N), 7.58–7.55 (m, 2H), 7.50–7.47 (m, 3H), 7.42 (d, *J* = 2.4 Hz, 1H), 3.89–3.72 (m, 2H, CH_2OH), 3.13–3.09 (m, 1H, *CH*-N), 2.00–1.91 [m, 1H, $CH(CH_3)_2$], 0.95 [t, 6H, $CH(CH_3)_2$]. ^{13}C NMR ($CDCl_3$): δ 164.8 (CH=N), 158.0 (*C*–OH), 135.3, 135.3, 133.2, 131.4, 130.9, 121.9, 120.1, 110.1, 76.7 (CH–N), 64.4 (CH_2OH), 30.0 [$CH(CH_3)_2$], 19.8 and 18.6 [2C, $CH(CH_3)_2$], MS (API-ES): *m/z* 439.9 $[M - H]^-$, 475.9 $[M + Cl]^-$.

(*S*)-2-[*N*-3-(4-bromophenyl)-5-bromosalicylidene]-amino-3,3-dimethyl-1-butanol (**L**[7]): yellow solid, yield 74%; m.p. 57–60 °C. $[\alpha]_{589}^{23} = -25.6°$ (*c* 0.0015, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 14.20 (s, 1H, O*H*), 8.33 (s, 1H, C*H*=N), 7.58–7.55 (m, 2H), 7.50–7.47 (m, 3H), 7.42 (d, 1H), 4.13–3.68 (m, 2H, CH_2OH), 3.00–2.97 (m, 1H, *CH*-N), 0.96 (s, 9H, $[C(CH_3)_3]$. ^{13}C NMR ($CDCl_3$): δ 164.8 (CH=N), 158.0 (*C*–OH), 135.3, 135.3, 133.3, 131.4, 130.9, 130.8, 121.9, 120.1, 110.2, 81.0 (*CH*-N), 62.3 (CH_2OH), 33.21 [$C(CH_3)_3$], 27.0 [3C, $C(CH_3)_3$]. MS (APCI): *m/z* 453.9 $[M + H]^+$.

General procedure for asymmetric oxidation of aryl methyl sulfides

The compound $VO(acac)_2$ (2.7 mg, 0.01 mmol) and a chiral Schiff base ligand in a required amount were dissolved in CH_2Cl_2 (1 ml), and the clear blue solution was stirred at room temperature for 10 min. Sulfide (1 mmol) in CH_2Cl_2 (1 ml) was then added to the solution, followed by the dropwise addition of aqueous H_2O_2 (30%, 1.15 mmol) at 0 °C. The mixture was stirred for 8 h at 0 °C. The resulting solution was extracted with CH_2Cl_2 (3×15 ml), and then washed with brine. The organic layer was dried over anhydrous $MgSO_4$, and the filtrate was concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel with petroleum ether–ethyl acetate (1 : 5, v/v) as eluent. The enantiomeric excess of the sulfoxide was determined by HPLC analysis [$C_6H_5S(O)CH_3$ and 2-$C_{10}H_7S(O)CH_3$: Daicel chiralcel OD-H, *n*-hexane–*i*-PrOH 9 : 1; 4-$BrC_6H_4S(O)CH_3$: Daicel chiralcel OB-H, *n*-hexane–*i*-PrOH 8 : 2; 4-$CH_3OPhSOCH_3$: *n*-hexane–*i*-PrOH 5 : 5].

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