Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Synthesis of Chiral Sulfamide-Amine Alcohol Ligands for Enantioselective Alkylation of Aldehydes

Jincheng Mao [a]

[a] Key Laboratory of Organic Synthesis of Jiangsu Province, College of Chemistry, Chemical Engineering and Materials Science, Suzhou University, Suzhou, China

Available online: 08 Sep 2009

To cite this article: Jincheng Mao (2009): Synthesis of Chiral Sulfamide-Amine Alcohol Ligands for Enantioselective Alkylation of Aldehydes, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 39:20, 3710-3721

To link to this article: http://dx.doi.org/10.1080/00397910902806265

Synthetic Communications®, 39: 3710–3721, 2009

ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910902806265

Taylor & Francis
Taylor & Francis Group

Synthesis of Chiral Sulfamide–Amine Alcohol Ligands for Enantioselective Alkylation of Aldehydes

Jincheng Mao
Key Laboratory of Organic Synthesis of Jiangsu Province, College of Chemistry, Chemical Engineering and Materials Science, Suzhou University, Suzhou, China

Abstract: A series of chiral sulfamide–amine alcohols (SAA) (**1–6**) has been easily synthesized from commercially available chiral amino alcohols. In the absence of $Ti(O^iPr)_4$, ligand **4** catalyzed the asymmetric addition of diethylzinc to aromatic aldehydes with moderate to good yields and enantioselectivities.

Keywords: Amine alcohols, asymmetric addition, diethylzinc, enantioselectivities

INTRODUCTION

Optically active secondary alcohols are important building blocks for the synthesis of many optically and biologically active compounds.[1] The enantioselective addition of organozinc reagents to carbonyl compounds represents one of the most useful ways, because of its simultaneous formation of a new C-C bond and a stereogenic center in one step. Thus, the development of various chiral ligands as catalysts for the enantioselective alkylation has gained considerable significance over the past two decades.[2–5] For these reactions to be successfully exploited in large-scale applications, the chiral ligands shoud be readily available or

Received June 27, 2008.
Address correspondence to Jincheng Mao, Key Laboratory of Organic Synthesis of Jiangsu Province, College of Chemistry, Chemical Engineering and Materials Science, Suzhou University, Suzhou 215 123, China. E-mail: jcmao@suda.edu.cn

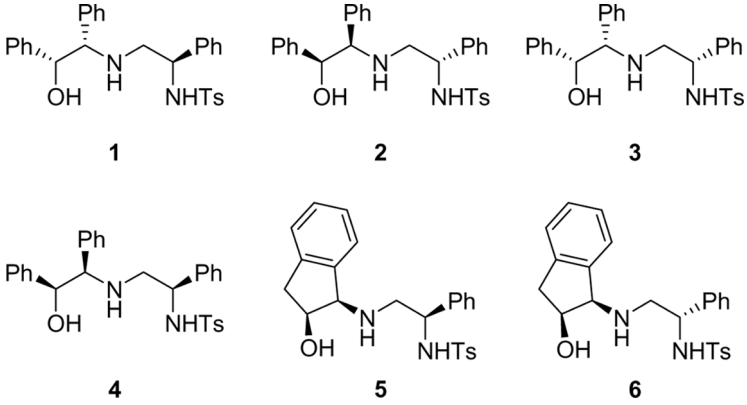
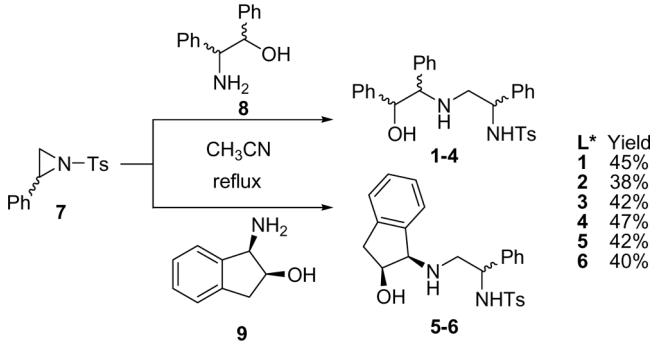


Figure 1. Evaluated ligands in the study.

easily recycled. However, from the relevant reviews,[3] it can be seen that only a small number of effective ligands were obtained by simple synthetic methods. As to the catalytic reaction, an additional Lewis acid such as $Ti(O^iPr)_4$ is always required for high efficiency. There is no doubt that the addition of the moisture-sensitive $Ti(O^iPr)_4$ will increase the cost and operational difficulty of the catalytic reaction. Therefore, stable, easily accessible, and operationally simple ligands are still desirable for the enantioselective alkylation without using $Ti(O^iPr)_4$. From the published papers, it can be seen that $Ti(O^iPr)_4$ is necessary for the asymmetric catalytic reaction promoted by chiral sulfonamide ligands.[6–9] In contrast, we have conveniently prepared a novel type of chiral sulfamide–amine alcohols (SAA) for highly enantioselective addition of diethylzinc to both aromatic and aliphatic or α,β-unsaturated aldehydes without using $Ti(O^iPr)_4$.[10,11] As part of further extending the application of our methodology, in this article, we report our finding of another series of chiral SAA (**1–6**) (Fig. 1) for the asymmetric addition of diethylzinc to aldehydes in the absence of $Ti(O^iPr)_4$.

RESULTS AND DISCUSSION

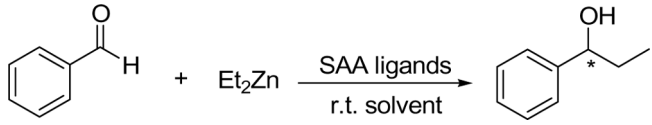
SAA ligands were easily prepared from the corresponding chiral aziridine (**7**) and chiral amino alcohols (**8** and **9**) in one step in an atom-economical synthesis (Scheme 1). Notably, **7** was also conveniently synthesized from commercially available chiral phenylglycinol.[12] As shown, the desired chiral compounds were obtained by simple flash-column chromatography in moderate yields (38–47%). Meanwhile, these ligands are stable



Scheme 1. Synthesis of the novel SAA ligands.

for several months in air. Given our interest in stereoselective reactions,[13] we decided to investigate the catalytic property of these chiral compounds as ligands in asymmetric catalysis. The asymmetric addition of diethylzinc to benzaldehyde, which has been considered a typical catalytic asymmetric benchmark reaction, was chosen as the model reaction. The relevant results are listed in Table 1. It can be seen that ligand **4** induced the catalytic reaction with best enantioselectivity

Table 1. Asymmetric addition of diethylzinc to benzaldehyde using SAA ligands **1–6**[a]



Entry	Ligand	Solvent	Time (h)	Ee (%)[b]	Config.[c]
1	**1**	Toluene	24	15	*R*
2	**2**	Toluene	24	34	*S*
3	**3**	Toluene	24	52	*R*
4	**4**	Toluene	24	62	*S*
5	**5**	Toluene	24	28	*R*
6	**6**	Toluene	24	46	*S*
7	**6**	Hexane	24	30	*S*

[a]Et_2Zn/aldehyde/ligand = 2.2:1:0.1; 24 h. In all cases, the isolated yield of the corresponding chiral secondary alcohol was 90–99%.

[b]The ee values were determined by GC.

[c]The absolute configuration assigned by comparison to literature values.

(62% ee) (Table 1, entry 4). Notably, chiral ligands (**1**–**6**) with different matching of stereogenic configurations gave the corresponding chiral products with different configurations. It can be concluded that this difference is possibly attributed to the configuration of the chiral aziridine used. By scanning the published papers, we can see that either toluene or hexane is considered the best solvent for asymmetric addition of diethylzinc to aldehydes. However, hexane was not a suitable solvent for our catalytic system (entry 7).

It is well known that the additives have an important role in the catalytic reactions.[14] Thus, various additives were employed, such as DMAP (4-dimethylaminopyridine), imidazole, TMSCl (trimethyl chlorosilane), Et_3N, and DiMPEG (dimethoxy polyethylene glycol, $M_n = 2000$).[15] Generally, dissapointing results were obtained (Table 2, entries 2–6).

With the optimal condition in hand, various aromatic aldehydes were used as the substrates in the catalytic reaction. The relevant results are listed in Table 3. It can be seen that donor group in the *para*-position of the aromatic ring was unfavorable for the enantioselectivity (Table 3, entry 6). Generally, the chiral ligand **4** showed good chemical selectivities and moderate enantioselectivities in the asymmetric ethylation of aromatic aldehydes. The good enantioselectivity was obtained when 2-fluorobenzaldehyde was investigated as the substrate (entry 2). When the asymmetric addition of diethylzinc to 2-naphthaldehyde was performed at 0°C, the corresponding chiral product was obtained with 70% ee (entry 11).

Table 2. Additive-mediated asymmetric addition of diethylzinc to benzaldehyde induced by **4**[a]

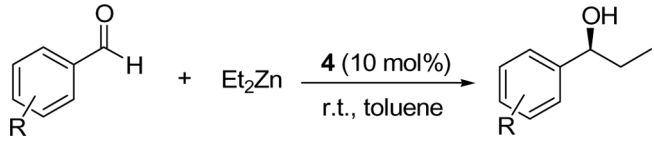
Entry	Ligand	Additive	Ee (%)[b]	Config.[c]
1	**4**	—	62	*S*
2	**4**	DMAP	6	*S*
3	**4**	Imidazole	40	*S*
4	**4**	TMSCl	1	—
5	**4**	Et_3N	2	—
6	**4**	DIMPEG	52	*S*

[a]Et_2Zn/aldehyde/ligand = 2.2:1:0.1; 24 h. In all cases, the isolated yield of the corresponding chiral secondary alcohol was 90–99%.

[b]The ee values were determined by GC.

[c]The absolute configuration assigned by comparison to literature values.

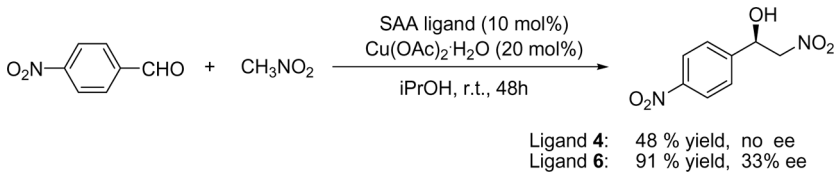
Table 3. Asymmetric addition of diethylzinc to various aromatic aldehydes induced by **4**[a]



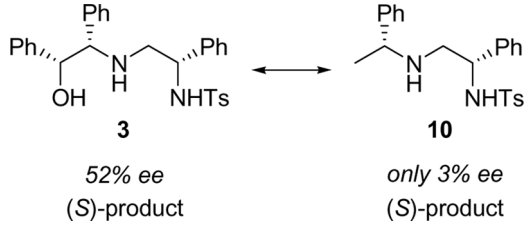
Entry	Substrates	Yield (%)[b]	Ee (%)[c]	Config.[d]
1	Benzaldehyde	99	62	*S*
2	2-Fluorobenzaldehyde	98	66	*S*
3	2-Chlorobenzaldehyde	85	63	*S*
4	3-Chlorobenzaldehyde	71	46	*S*
5	4-Chlorobenzaldehyde	91	50	*S*
6	4-Bromobenzadehyde	82	52	*S*
7	4-Tolualdehyde	67	48	*S*
8	4-(Trifluoromethyl)benzaldehyde	95	62	*S*
9	1-Naphthaldehyde	74	33	*S*
10	2-Naphthaldehyde	97	50	*S*
11[e]	2-Naphthaldehyde	83	70	*S*

[a]Et_2Zn/aldehyde/ligand = 2.2:1:0.1; hexane, rt, 24 h.
[b]Isolated yield.
[c]The ee values were determined by GC.
[d]The absolute configuration assigned by comparison with literature values.
[e]The catalytic reaction was performed at 0 °C.

To prove the efficiency of our catalytic system, it was applied to a copper-catalyzed asymmetric Henry reaction. To our astonishment, we got only the racemic product when the SAA ligand **4** was used (Scheme 2). However, under the nonoptimized conditions, the corresponding chiral secondary alcohol was obtained in 91% yield with promising enantioselectivity (33% ee) when **6** was employed as the chiral ligand. This showed that the catalytic reactivity of the chiral ligand in the



Scheme 2. Asymmetric Henry reaction catalyzed by $Cu(OAc)_2 \cdot H_2O$–SAA ligands (**4** and **6**).



Scheme 3. Difference of the ligands' structure (**3** and **10**) led to the changing of the enantioselectivities in the catalytic reaction.

asymmetric Henry reaction was completely dependent on the structure of the chiral ligand itself. Thus, it was encouraging that our catalytic system could be efficient in other asymmetric transition processes. Further work is under way in our laboratory.

In consideration of the possible mechanism, a similar ligand, **10**, was synthesized for the comparison with ligand **3** and then applied to the asymmetric ethylation reaction. The (*S*)-product was obtained with only 3% ee when **10** was used (Scheme 3). This result suggested that the hydroxyl group was essential for the catalytic efficiency.

On the basis of the well-known mechanism for asymmetric alkylation of aldehydes with diethylzinc,[16,17] plausible canonical *anti* transition states are proposed when the SAA ligands derived from different chiral amino alcohols were used[18–21] (Fig. 2). Both the N-atom and the

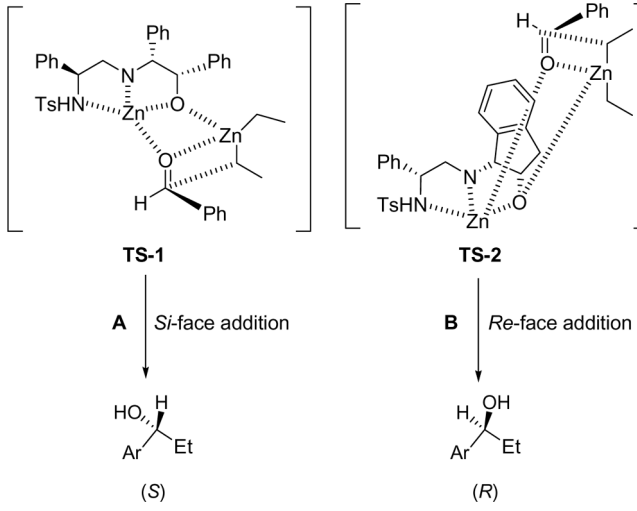


Figure 2. Proposed transition states.

O-atom of the amino alcohol, along with the N-atom from the sulfonamide group, participate in the coordination with Zn to form an *O,N,N*-chelating tridentate complex. From the catalytic efficiency of SAA ligands, we can reason that the N-atom from the sulfonamide servers as another weakly coordinative site in the cycle because it is a poor electron donor.[22] Thus, based on the transition states **TS-1** and **TS-2** as the catalytically active species, the SAA ligand **4** affords the (*S*)-enantiomer of the product, and the SAA ligand **5** yields the (*R*)-enantiomer.

CONCLUSIONS

In summary, the novel sulfamide–amine alcohol ligands were readily prepared in moderate yields in short synthetic sequences. These ligands were evaluated in the asymmetric addition of diethylzinc to aldehydes, which provided the chiral secondary alcohols with excellent yields and good enantioselectivities in the absence of $Ti(O^iPr)_4$. Further work is in progress in our laboratory with the aim of expanding the use of these inexpensive chiral compounds to other enantioselective processes. Experiments are under way to prove our plausible mechanism for the asymmetric alkynylzinc addition of aldehydes.

EXPERIMENTAL

General

All reactions were carried out under an argon atmosphere. Solvents were dried and degassed by the standard methods and organozinc reagent and all aldehydes were purchased from Aldrich and Alfa. Flash-column chromatography was performed by using silica gel (300–400 mesh). Analytical thin-layer chromatography (TLC) was performed by using glass plates precoated with 200- to 400-mesh silica gel impregnated with a fluorescent indicator (254 nm). NMR spectra were measured in $CDCl_3$ on a Varian Inova-400 NMR spectrometer (400 MHz or 300 MHz) with tetramethylsilane (TMS) as an internal reference. Enantiomeric excess (*ee*) determination was carried out using gas chromatography (GC) with a chiral cyclodex β-2, 3, 6-M, 30-m $\times$ 0.32-mm capillary column on an Agilent HP-4890 GC instrument with flame ionization detector (FID), and high-performance liquid chromatography (HPLC) was done with a chiral OD-H column. High-resolution mass spectra (HRMS) were measured with electron impact (EI).

General Procedure for Preparation of Sulfamide–Amine Alcohol 1

(*S*)-2-Phenyl-1-tosylaziridine **7** (1.0 g, 3.66 mmol) and chiral amino alcohol **8** (0.8 g, 3.80 mmol) were dissolved in dry acetonitrile (30 mL), and the mixture was stirred under reflux for 18 h. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (eluent:petroleum ether/ethyl acetate = 1/1) to give the corresponding ligand **1** as white solid (0.8 g), 45% yield. Ligands **2–4** were prepared analogously.

When (1*R*,2*S*)-cis-1-amino-2-indanol (**9**) was used as the chiral amino alcohol, ligands **5** and **6** were obtained with this procedure.

When (*R*)-1-phenylethanamine was employed instead of the chiral amino alcohol, ligand (**10**) was obtained.

Data

Ligand **1**

White solid, 45% yield, $[\alpha]_D^{25} = -26.3$ (c = 2.0 in MeOH); ^{1}H NMR ($CDCl_3$) δ: 2.35 (s, 3H), 2.52 (d, $J = 7.2$ Hz, 2H), 3.62 (d, $J = 8.4$ Hz, 1H), 4.18 (s, 1H), 4.68 (d, $J = 8.8$ Hz, 1H), 5.55 (s, 1H), 6.96–6.99 (m, 2H), 7.07–7.14 (m, 8H), 7.22–7.30 (m, 7H), 7.46 (d, $J = 10.8$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ: 21.9, 52.9, 57.5, 69.4, 77.8, 126.9, 127.1, 127.5, 127.9, 128.3, 128.3, 128.6, 128.8, 129.8, 137.7, 139.4, 139.5, 140.8, 143.4; MS m/z: 379.1484 (69, M–C_7H_7O), 155.0206 (80, $C_7H_7O_2S$), 106.0420 (55, C_7H_6O), 105.0337 (66, C_7H_6O), 91.0564 (100, C_7H_7).

Ligand **2**

White solid, 38% yield, $[\alpha]_D^{25} = +27.2$ (c = 2.0 in MeOH); ^{1}H NMR ($CDCl_3$) δ: 2.35 (s, 3H), 2.52 (d, $J = 7.6$ Hz, 2H), 3.63 (d, $J = 8.4$ Hz, 1H), 4.18 (s, 1H), 4.69 (d, $J = 8.4$ Hz, 1H), 5.51 (s, 1H), 6.96–6.99 (m, 2H), 7.07–7.14 (m, 11H), 7.23–7.37 (m, 4H), 7.46 (d, $J = 11.2$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ: 21.9, 52.9, 57.5, 69.3, 77.8, 126.9, 127.1, 127.5, 127.9, 128.3, 128.6, 128.8, 129.8, 137.7, 139.5, 140.8, 143.4; MS m/z: 379.1485 (69, M–C_7H_7O), 155.0208 (75, $C_7H_7O_2S$), 106.0411 (51, C_7H_6O), 105.0347 (63, C_7H_6O), 91.0554 (100, C_7H_7).

Ligand **3**

White solid, 42% yield, $[\alpha]_D^{25} = +18.6$ (c = 3.0 in MeOH); ^{1}H NMR ($CDCl_3$) δ: 2.36 (s, 3H), 2.58 (d, $J = 8.4$ Hz, 1H), 2.71 (d, $J = 8.0$ Hz, 1H), 3.88 (s, 1H),

4.31 (s, 1H), 4.88 (s, 1H), 5.92 (brs, 2H), 6.95–7.03 (m, 4H), 7.09–7.24 (m, 12H), 7.55 (d, $J = 8.0$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ: 21.9, 52.4, 57.2, 68.1, 77.0, 127.0, 127.2, 127.6, 127.9, 128.0, 128.2, 128.4, 128.7, 128.7, 129.8, 137.8, 139.1, 140.7, 143.5; MS m/z: 379.1491 (56, M–C_7H_7O), 155.0195 (74, $C_7H_7O_2S$), 106.0421 (36, C_7H_6O), 105.0350 (47, C_7H_6O), 91.0559 (100, C_7H_7).

Ligand **4**

White solid, 47% yield, $[\alpha]_D^{25} = -25.0$ (c = 2.0 in MeOH); ^{1}H NMR ($CDCl_3$) δ: 1.80 (brs, 2H), 2.37 (s, 3H), 2.55 (d, $J = 8.4$ Hz, 1H), 2.66 (d, $J = 9.0$ Hz, 1H), 3.80 (s, 1H), 4.27 (s, 1H), 4.80 (s, 1H), 5.68 (brs, 1H), 6.95–7.26 (m, 13H), 7.54 (d, $J = 5.1$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ: 21.9, 52.6, 57.4, 68.3, 77.4, 127.0, 127.2, 127.6, 127.9, 128.2, 128.5, 128.6, 128.8, 128.8, 137.8, 138.5, 139.3, 140.8, 143.5; MS m/z: 379.1494 (60, M–C_7H_7O), 155.0198 (78, $C_7H_7O_2S$), 106.0414 (47, C_7H_6O), 105.0347 (57, C_7H_6O), 91.0558 (100, C_7H_7).

Ligand **5**

White solid, 42% yield, $[\alpha]_D^{25} = -1.5$ (c = 2.3 in MeOH); ^{1}H NMR ($CDCl_3$) δ: 1.92 (brs, 2H), 2.36 (s, 3H), 2.86–3.12 (m, 4H), 3.97 (d, $J = 6.4$ Hz, 1H), 4.35–4.43 (m, 2H), 5.30 (s, 1H), 7.14–7.22 (m, 11H), 7.61 (d, $J = 10.8$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ: 20.9, 30.7, 52.9, 57.7, 65.3, 70.9, 124.3, 124.8, 125.9, 126.4, 126.8, 127.0, 127.9, 129.2, 138.7, 140.8, 140.9, 142.1, 143.5; MS m/z: 379.1490 (7, M–C_2H_3O), 155.0209 (75, $C_7H_7O_2S$), 106.0414 (47, C_7H_6O), 129.0614 (71, C_9H_7N), 91.0556 (100, C_7H_7).

Ligand **6**

White solid, 40% yield, $[\alpha]_D^{25} = +40.5$ (c = 2.0 in MeOH); ^{1}H NMR ($CDCl_3$) δ: 1.71 (brs, 2H), 2.34 (s, 3H), 2.85–3.11 (m, 4H), 3.95 (d, $J = 4.8$ Hz, 1H), 4.38–4.43 (m, 2H), 5.48 (s, 1H), 7.11–7.27 (m, 11H), 7.59 (d, $J = 10.2$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ: 21.9, 40.1, 53.8, 58.0, 65.9, 71.8, 124.7, 126.0, 127.2, 127.3, 127.6, 128.2, 128.6, 129.0, 129.9, 137.6, 138.5, 141.0, 142.3, 143.7.

Ligand **10**

White solid, 55% yield; ^{1}H NMR ($CDCl_3$) δ: 1.27 (d, $J = 5.1$ Hz, 3H), 2.37 (s, 3H), 2.52–2.81 (m, 2H), 3.53–3.57 (m, 1H), 4.27–4.30 (m, 1H), 7.06–7.32 (m, 12H), 7.60 (d, $J = 5.7$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ: 21.9,

24.5, 52.7, 57.1, 57.5, 126.8, 127.1, 127.6, 127.7, 127.9, 128.7, 129.1, 129.8, 137.7, 139.6, 143.6, 144.7.

General Procedures for the Asymmetric Addition of Et_2Zn to Aldehydes

Under a dry argon atmosphere, chiral ligand (10 mol%, 0.05 mmol) in dry toluene (4 mL) was cooled to 0°C and a solution of Et_2Zn (1.0 M in hexane, 1.1 mmol) was added slowly. After stirring for 30 min at 0°C, freshly distilled aldehyde (0.5 mmol) was added, and the reaction was stirred for 24 h at 10°C. The reaction mixture was quenched with 1 N aqueous HCl at 0°C. The aqueous phase was extracted with ethyl acetate (3×5 mL). The combined organic phase was washed with little brine, dried with anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by flash-column chromatography on silica gel (petroleum ether–ethyl acetate = 12:1) to give the carbinol. The enantiomeric purity of the product was determined by HPLC. The absolute configurations of the products were assigned by comparison to literature values.

General Procedures for the Asymmetric Henry Reaction Between 4-Nitrobenzaldehyde and Nitromethane

Chiral ligand (10 mol%, 0.02 mmol) and $Cu(OAc)_2 \cdot H_2O$ (4.0 mg, 0.02 mmol) were added to isopropanol (2.0 mL) at room temperature in air. The reaction mixture was stirred for 30 min, and then 4-nitrobenzaldehyde (30.2 mg, 0.2 mmol) and nitromethane (0.3 mL) were added to the resulting blue solution. The mixture was stirred for 48 h at room temperature and then concentrated in vacuo to give a glutinous phase residue. Next, CH_2Cl_2 (2.0 mL) and aqueous HCl solution (1.0 M, 5 mL) were added into the residue, and the mixture was stirred until the green color disappeared. After extraction with CH_2Cl_2 (3×10 mL), the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and evaporated in vacuo. The residue was purified by flash chromatography on silica gel (petroleum ether–ethyl acetate = 8:1) to afford the corresponding chiral product.

Data

2-Nitro-1-(4-nitrophenyl)ethanol

Yield 91%. Ee (33%) determined by HPLC analysis (Chiralcel OD-H column, IPA–hexane = 8:92). Retention time: $t_{major} = 16.71$ min, $t_{minor} = 18.64$ min.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.23 (d, $J = 4.0$ Hz, 1H), 4.57 (dd, $J = 4.0$, 13.8 Hz, 1H), 4.61 (dd, $J = 8.4$, 13.6 Hz, 1H), 5.62 (dd, $J = 3.6$, 12.0 Hz, 1H), 7.63 (d, $J = 8.8$ Hz, 2H), 8.28 (d, $J = 8.8$ Hz, 2H).

ACKNOWLEDGMENTS

We are grateful to the grants from the National Natural Science Foundation of China (No. 20802046) and the Key Laboratory of Organic Synthesis of Jiangsu Province for financial support.

REFERENCES

1. (a) Soai, K.; Shibata, T. In *Comprehensive Asymmetric Catalysis*; E.N. Jacobsen, A. Pfaltz, H. Yamamoto, (Eds.); Springer: Berlin, 1999; pp. 911–922; (b) Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; Wiley: New York, 1994; (c) Ojima, I. *Catalytic Asymmetric Synthesis,* 2nd ed.; Wiley-VCH: New York, 2000.
2. Brunner, H.; Zettlmeier, W. *Handbook of Enantioselective Catalysis*; VCH: New York, 1993; vols. 1–2.
3. Pu, L.; Yu, H. B. Catalytic asymmetric organozinc additions to carbonyl compounds. *Chem. Rev.* **2001**, *10*, 757.
4. Soai, K.; Niwa, S. Enantioselective addition of organozinc reagents to aldehydes. *Chem. Rev.* **1992**, *92*, 833.
5. Noyori, R.; Kitamura, M. Enantioselective addition of organometallic reagents to carbonyl compounds: Chirality transfer, multiplication, and amplification. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 49.
6. Balsells, J.; Walsh, P. J. Design of diastereomeric self-inhibiting catalysts for control of turnover frequency and enantioselectivity. *J. Am. Chem. Soc.* **2000**, *122*, 3250.
7. Ramón, D. J.; Yus, M. First enantioselective addition of dialkylzinc to ketones promoted by titanium (IV) derivatives. *Tetrahedron Lett.* **1998**, *39*, 1239.
8. Hwang, C. D.; Uang, B. J. Enantioselective addition of diethylzinc to aldehydes induced by a new chiral Ti(IV) catalyst. *Tetrahedron: Asymmetry* **1998**, *9*, 3979.
9. Ito, K.; Kimura, Y.; Okamura, H.; Katsuki, T. Enantioselective addition of diethylzinc to aldehydes in the presence of chiral titanium reagent modified with *n*-sulfonylated amino alcohol. *Synlett* **1992**, 573.
10. Mao, J.; Wan, B.; Wang, R.; Wu, F.; Lu, S. Concise synthesis of novel practical sulfamide–amine alcohols for the enantioselective addition of diethylzinc to aldehydes. *J. Org. Chem.* **2004**, *69*, 9123.
11. Mao, J.; Wan, B.; Zhang, Z.; Wang, R.; Wu, F.; Lu, S. Reversal of enantioselectivity by adding $Ti(OiPr)_4$: Novel sulfamide–amine alcohol ligands for

the catalytic asymmetric addition of diethylzinc to aldehydes. *J. Mol. Catal. A: Chem.* **2005**, *225*, 33.
12. Bieber, L. W.; de Araújo, M. C. F. Short and efficient synthesis of optically active n-tosyl aziridines from 2-amino alcohols. *Molecules* **2002**, *7*, 902.
13. (a) Xu, Z.; Mao, J.; Zhang, Y. Highly enantioselective alkynylation of aldehydes catalyzed by a new oxazolidine–titanium complex. *Org. Biomol. Chem.* **2008**, *6*, 1288; (b) Mao, J.; Wan, B.; Wu, F.; Lu, S. First example of asymmetric transfer hydrogenation in water induced by a chiral amino alcohol hydrochloride. *Tetrahedron Lett.* **2005**, *46*, 7341; (c) Mao, J.; Wan, B.; Wu, F.; Wang, R.; Lu, S. Sulfamide–amine alcohol catalyzed enantioselective alkynylation of aromatic ketones. *J. Mol. Catal. A: Chem.* **2005**, *237*, 126; (d) Mao, J.; Wan, B.; Wu, F.; Lu, S. Readily available sulfamide–amine alcohols for enantioselective phenylacetylene addition to aldehydes in the absence of $Ti(O^iPr)_4$. *Chirality* **2005**, *17*, 245.
14. Vogl, E. M.; Groger, H.; Shibasaki, M. Towards perfect asymmetric catalysis: additives and cocatalysts. *Angew. Chem. Int. Ed.* **1999**, *38*, 1570.
15. Bolm, C.; Rudolph, J. Catalyzed asymmetric aryl transfer reactions to aldehydes with boronic acids as aryl source. *J. Am. Chem. Soc.* **2002**, *124*, 14850.
16. Kitamura, M.; Suga, S.; Oka, H.; Noyori, R. Quantitative analysis of the chiral amplification in the amino alcohol–promoted asymmetric alkylation of aldehydes with dialkylzincs. *J. Am. Chem. Soc.* **1998**, *120*, 9800.
17. Yamakawa, M.; Noyori, R. Asymmetric addition of dimethylzinc to benzaldehyde catalyzed by (2*S*)-3-*exo*-(dimethylamino)isobornenol: A theoretical study on the origin of enantioselection. *Organometallics* **1999**, *18*, 128.
18. Huang, J.; Lanni, J. C.; Antoline, J. E.; Hsung, R. P.; Kozlowski, M.C. De novo chiral amino alcohols in catalyzing asymmetric additions to aryl aldehydes. *Org. Lett.* **2006**, *8*, 1565.
19. Rasmussen, T.; Norrby, P. O. Modeling the stereoselectivity of the β-amino alcohol-promoted addition of dialkylzinc to aldehydes. *J. Am. Chem. Soc.* **2003**, *125*, 5130.
20. Vazquez, J.; Pericas, M. A.; Maseras, F.; Lledos, A. A quantum mechanics/molecular mechanics study of the highly enantioselective addition of diethylzinc to benzaldehyde promoted by (*R*)-2-piperidino-1,1,2-triphenylethanol. *J. Org. Chem.* **2000**, *65*, 7303.
21. Goldfuss, B.; Houk, K. N. Origin of enantioselectivities in chiral β-amino alcohol catalyzed asymmetric additions of organozinc reagents to benzaldehyde: PM3 transition state modeling. *J. Org. Chem.* **1998**, *63*, 8998.
22. Pritchett, S.; Gantzel, P.; Walsh, P. J. Synthesis and crystal structures of chiral titanium bis(sulfonamido) bis(amide) complexes: Differences in ligand hapticity caused by crystal packing forces. *Organometallics* **1997**, *16*, 5130.