The Syntheses of new Camphorsulfonylated Ligands Derived from 2-Amino-2′-Hydroxy-1,1′-Binaphthyl and Their Enantioselectivities in the Addition of Dialkylzinc Reagents to Aldehydes

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ABSTRACT A series of new camphorsulfonylated ligands derived from chiral 2-amino-2′-hydroxy-1,1′-binaphthyl (NOBIN) and (+)-camphorsulfonic acid were synthesized by a short and simple synthetic sequence, and their enantioselective catalytic activities were assessed in the nucleophilic addition reaction of dialkylzinc reagents to aldehydes in the presence of titanium tetraisopropoxide. The most efficient ligand, *N*-hydroxycamphorsulfonylated (*S*)-NOBIN, gave (*S*)-addition products with good yields and up to 87% of ee value. The ^{1}H nuclear magnetic resonance (NMR) and ^{13}C NMR results of the titanium titration experiments on this ligand indicate that the most likely catalytic reactive species involved in this catalytic asymmetric addition is a bimetallic titanium complex. A possible catalytic reaction mechanism is proposed. *Chirality 00:000–000, 2012.*

KEY WORDS: camphorsulfonamide; titanium complex; asymmetric catalysis; dialkylzinc addition

INTRODUCTION

The stereoselective nucleophilic addition of organometallic reagents to aldehydes or ketones is an efficient and versatile method to generate chiral alcohols. These alcohols are not only components of many naturally occurring biologically active compounds but also valuable intermediates for the syntheses of other functionalities, such as halides, amides, esters, and ethers.[1] Concerning this subject, the asymmetric addition of organozinc reagents to carbonyl groups has been extensively investigated, and numerous chiral ligands containing a variety of structures have been developed.[2] Despite significant efforts so far, the development of new high efficient catalytic system remains as enduring interest.

Since Ramón and Yus firstly reported several camphorsulfonamide ligands promoting addition of dialkylzincs to aldehydes and ketones in the presence of titanium alkoxide,[3–5] many camphorsulfonamide ligands derived from various aliphatic and aromatic monoamines and diamines have been tested in the addition of dialkylzinc reagents to carbonyl groups with varying success in the presence of titanium alkoxide.[6–28] Among these ligands, Walsh's HOCSAC, a bis (hydroxycamphorsulfonamide) ligand derived from (*R*,*R*)-1,2-cyclohexyl diamine, has been shown to be the best one so far to give excellent results with up to 99% ee value using only 2% catalyst loading. Compared with the diverse camphorsulfonamides derived from monoamines and diamines, the camphorsulfonamide ligands derived from amino alcohols have rarely emerged.[29–31]

According to the investigations by others, the design of camphorsulfonamide ligand has been based on the mechanism that the bimetallic titanium complexes are the active catalytic species,[5,18,28] which have both a highly electrophilic, pentacoordinated, positively charged titanium center and a highly nucleophilic, hexacoordinated, negatively charged titanium center.[32] The two titanium centers are bridged with the flexible alkoxide, whose flexibility is likely to decrease enantioselectivity. We assume that a more rigid catalyst structure could be expected to give higher enantioselectivity. With the use of the synergistic coordination of phenolate oxygen atom with titanium, 2-amino-2′-hydroxy-1,1′-binaphthyl (NOBIN) may replace the flexible alkoxide bridge and generate a more rigid catalyst structure. To verify our assumption, we report our investigation on the syntheses of new chiral camphorsulfonamides derived from NOBIN and the studies of their enantioselective catalytic activities in the addition of dialkylzinc reagents to aldehydes.

EXPERIMENTAL

General Information

Rotations were measured on SGW-1 automatic polarimeter (Precision Scientific Instrument Co., Ltd., Shanghai, China). The ^{1}H nuclear magnetic resonance (NMR) and ^{13}C NMR spectra were recorded on a Bruker Avance 400 MHz spectrometer (Switzerland). Elemental analyses were performed on Vario MICRO CHONS analyzer (Germany ELEMENTAR). Electrospray ionization mass spectrometry (ESI-MS) spectra were obtained at 70 eV on a Thermo Finnigan DECAX-30000 LCQ Deca XP spectrometer (Switzerland) giving fragment ions in *m/z* with relative intensities (%) in parentheses. Gas chromatography (GC) analyses were performed on 9790 II chromatograph (Fuli Analytical Instrument Co., Ltd., Zhejiang, China) by using a Varian CP-Chirasil Dex CB column (25 m × 0.32 mm) (USA). All solvents used were dried and purified by using standard, published methods. All aldehydes, $NaBH_4$, and diethylzinc (1.5 M solution in toluene) were purchased from Acros and were used directly. Dimethylzinc (1.0 M solution in toluene) and

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(+)-(*S*)-10-camphorsulfonic acid were purchased from J&Kchemical and were used directly. $Ti(O^iPr)_4$ purchased from Aldrich was freshly distilled prior to use. (*R*)-NOBIN and (*S*)-NOBIN were prepared according to literature procedures.[33] Unless otherwise noted, all reactions were carried out under nitrogen atmosphere by using standard Schlenk and vacuum line techniques.

Preparation of Bisketocamphorsulfonylated NOBIN 1–2

General procedure of synthesis of the investigated sulfonamides is shown in Scheme 1. Initially, the (+)-(*S*)-10-camphorsulfonyl chloride was prepared from (+)-(*S*)-10-camphorsulfonic acid by reflux in $SOCl_2$. The investigated bisketocamphorsulfonylated NOBIN were obtained as follows: 17.5 mmol of Et_3N and 0.2 mmol of 4-(dimethylamino)pyridine (DMAP) were added to the solution of (*R*)-NOBIN and (*S*)-NOBIN (3.5 mmol) in tetrahydrofuran (THF) (20 ml) at room temperature, respectively, then (+)-(*S*)-10-camphorsulfonyl chloride (10.5 mmol) was added in portions at 0 °C and the reaction mixture was stirred for 2.5 h at room temperature. The reaction mixture was subsequently quenched by adding 100 ml of water, extracted by EtOAc (3 × 50 ml), washed by brine (50 ml), dried over anhydrous sodium sulfate, and filtered. The filtrate was concentrated in vacuo to give a residue, which was purified by column chromatography (eluting with *n*-hexane/EtOAc = 4/1) to provide the titled products correspondingly.

(R_a)-1-[2-({[(1*S*,4*R*)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl]methane}sulfonamido))naphthalen-1-yl])naphthalen-2-yl [(1*S*,4*R*)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl]methanesulfonate (1). Colorless solid (90%); $[\alpha]_D^{30}$ = +16.7 (c 0.6, THF); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.21 (d, *J* = 9.0 Hz, 1H, ArH), 8.12–8.06 (m, 2H, ArH), 8.00 (d, *J* = 8.2 Hz, 1H, ArH), 7.91 (d, *J* = 8.1 Hz, 1H, ArH), 7.79 (d, *J* = 9.0 Hz, 1H, ArH), 7.56–7.52 (t, 1H, ArH), 7.43–7.34 (m, 2H, ArH), 7.30–7.24 (m, 2H, ArH), 7.06 (d, *J* = 8.5 Hz, 1H, ArH), 6.87 (s, 1H, NH), 3.34 (d, *J* = 14.8 Hz, 1H, CH_2S), 3.18 (d, *J* = 14.9 Hz, 1H, CH_2S), 2.92 (d, *J* = 14.8 Hz, 1H, CH_2S), 2.34–2.18 (m, 4H, CH_2S, CH_2), 2.06–1.71 (m, 8H, CH_2, CH), 1.39–1.17 (m, 3H, CH_2), 0.96, 0.63, 0.59, 0.48 (s, 12H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 214.65, 213.05, 145.87, 134.53, 133.10, 133.05, 132.43, 131.24, 130.68, 130.32, 128.55, 128.11, 127.96, 127.23, 126.81, 125.95, 125.79, 125.29, 124.01, 121.91, 119.79, 119.77, 58.64, 57.56, 50.91, 49.16, 48.12, 47.57, 42.70, 42.58, 42.44, 42.18, 26.88, 26.73, 25.54, 24.50, 19.61, 19.50, 19.17, 19.13; ESI-MS calce for $[C_{40}H_{43}NO_7S_2 + Na]^+$ 736.24, found 736.3; *Anal*. Calcd for $C_{40}H_{43}NO_7S_2$: C, 67.30, H, 6.07, N, 1.96, O, 15.69, S, 8.98, Found: C, 66.88, H, 6.01, N, 1.87, O, 16.30, S, 8.69.

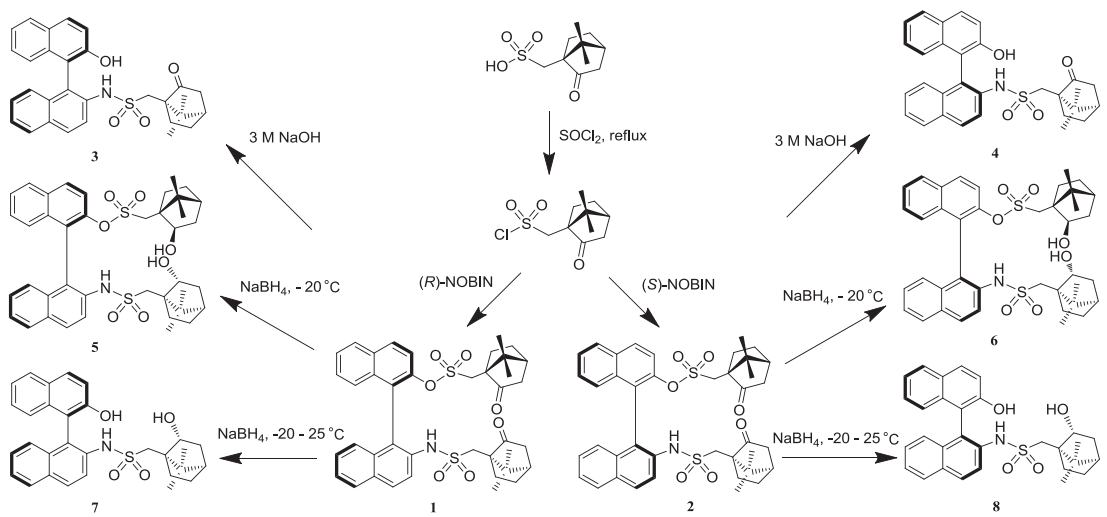
(S_a)-1-[2-({[(1*S*,4*R*)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl]methane}sulfonamido))naphthalen-1-yl])naphthalen-2-yl[(1*S*,4*R*)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl]methanesulfonate (2). Colorless solid (89%); $[\alpha]_D^{30}$ = +51.7 (c 0.7, THF); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.19–8.05 (m, 3H, ArH), 8.01 (d, *J* = 8.2 Hz, 1H, ArH), 7.92 (d, *J* = 8.1 Hz, 1H, ArH), 7.80 (d, *J* = 9.0 Hz, 1H, ArH), 7.56–7.52 (t, 1H, ArH), 7.45–7.36 (m, 2H, ArH), 7.33–7.26 (m, 2H, ArH), 7.09 (d, *J* = 8.4 Hz, 1H, ArH), 6.84 (s, 1H, NH), 3.52 (d, *J* = 14.9 Hz, 1H, CH_2S), 3.01 (d, *J* = 14.9 Hz, 1H, CH_2S), 2.72 (d, *J* = 14.9 Hz, 1H, CH_2S), 2.42 (d, *J* = 14.9 Hz, 1H, CH_2S), 2.28–1.24 (m, 14H, CH_2, CH), 0.96, 0.81, 0.72, 0.57 (s, 12H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 214.73, 213.12, 146.05, 134.37, 133.03, 132.43, 131.25, 130.73, 130.30, 128.52, 128.08, 127.91, 127.40, 126.78, 125.95, 125.70, 125.44, 123.95, 121.86, 120.18, 119.92, 58.57, 57.63, 50.98, 49.03, 48.07, 47.71, 42.75, 42.72, 42.40, 42.25, 26.80, 26.75, 25.45, 24.87, 19.72, 19.62, 19.37, 19.31; ESI-MS calce for $[C_{40}H_{43}NO_7S_2 + Na]^+$ 736.24, found 736.5; *Anal*. Calcd for $C_{40}H_{43}NO_7S_2$: C, 67.30, H, 6.07, N, 1.96, O, 15.69, S, 8.98, Found: C, 67.14, H, 5.97, N, 1.90, O, 16.05, S, 9.02.

Preparation of Mono-N-ketocamphorsulfonylated NOBIN 3–4

The general procedure of hydrolysis of **1–2** to give **3–4** is as follows: 4 ml of 3 M sodium hydroxide solution was added to the solution of bisketocamphorsulfonylated NOBIN **1–2** (1 mmol) in EtOH (10 ml) and THF (10 ml), respectively, then the reaction mixture was refluxed for 24 h. After completion, the reaction mixture was cooled to room temperature, quenched by adding 12 ml of 1 M hydrochloric acid, extracted with EtOAc (3 × 30 ml), washed by brine (30 ml), dried over anhydrous sodium sulfate, and filtered. The filtrate was concentrated in vacuo to give a residue, which was purified by column chromatography (eluting with *n*-hexane/EtOAc = 4/1) to give the corresponding titled products.

(R_a)-1-[(1*S*,4*R*)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl]-*N*-[1-(2-hydroxynaphthalen-1-yl)naphthalen-2-yl]methanesulfonamide (3). Colorless solid (96%); $[\alpha]_D^{30}$ = −18.2 (c 1.1, THF); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.15–8.08 (m, 2H, ArH), 7.99–7.95 (m, 2H, ArH), 7.91 (d, *J* = 8.0 Hz, 1H, ArH), 7.50–7.46 (t, 1H, ArH), 7.40–7.28 (m, 4H, ArH), 7.19 (d, *J* = 8.5 Hz, 1H, ArH), 7.03 (d, *J* = 8.4 Hz, 1H, ArH), 6.79 (s, 1H, NH), 5.56 (s, 1H, OH), 3.36 (d, *J* = 14.8 Hz, 1H, CH_2S), 2.82 (d, *J* = 14.8 Hz, 1H, CH_2S), 2.30–1.27 (m, 7H, CH_2, CH), 0.98, 0.64 (s, 6H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 215.52, 152.01, 134.86, 133.42, 133.23, 131.47, 131.28, 130.59, 129.47, 128.55, 128.37, 127.61, 127.43, 125.70, 125.52, 124.08, 124.00, 120.79, 120.18, 118.24, 113.22, 58.75, 50.49, 48.05, 42.75, 42.37, 26.79, 25.44, 19.66, 19.52; ESI-MS calce for $[C_{30}H_{29}NO_4S + Na]^+$ 522.17, found 522.3; *Anal*. Calcd for $C_{30}H_{29}NO_4S$: C, 72.12, H, 5.85, N, 2.80, O, 12.81, S, 6.42, Found: C, 71.99, H, 5.90, N, 2.68, O, 13.03, S, 6.32.

(S_a)-1-[(1*S*,4*R*)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl]-*N*-[1-(2-hydroxynaphthalen-1-yl)naphthalen-2-yl]methanesulfonamide (4). Colorless solid (94%); $[\alpha]_D^{30}$ = +69.3 (c 0.7, THF); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.15 (d, *J* = 9.0 Hz, 1H, ArH), 8.07 (d, *J* = 9.1 Hz,



Scheme 1. Preparation of camphorsulfonamides derived from 2-amino-2′-hydroxy-1,1′-binaphthyl.

1H, ArH), 7.98–7.90 (m, 3H, ArH), 7.48–7.27 (m, 5H, ArH), 7.18 (d, J = 8.5 Hz, 1H, ArH), 7.05 (d, J = 8.4 Hz, 1H, ArH), 6.76 (s, 1H, NH), 5.70 (s, 1H, OH), 3.46 (d, J = 14.9 Hz, 1H, CH_2S), 2.83 (d, J = 14.9 Hz, 1H, CH_2S), 2.30–1.26 (m, 7H, CH_2, CH), 0.97, 0.72 (s, 6H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 215.67, 151.96, 135.20, 133.24, 133.14, 131.38, 131.26, 130.67, 129.52, 128.53, 128.37, 127.62, 127.56, 125.63, 125.29, 124.13, 123.99, 119.85, 118.86, 118.07, 112.95, 58.67, 50.42, 48.23, 42.68, 42.43, 26.82, 25.22, 19.69, 19.62; ESI-MS calce for $[C_{30}H_{29}NO_4S + Na]^+$ 522.17, found 522.3; *Anal*. Calcd for $C_{30}H_{29}NO_4S$: C, 72.12, H, 5.85, N, 2.80, O, 12.81, S, 6.42, Found: C, 72.05, H, 5.75, N, 2.88, O, 12.70, S, 6.52.

Preparation of Bishydroxycamphorsulfonylated NOBIN 5–6

The general procedure of reduction of **1–2** to give **5–6** is as follows: $NaBH_4$ (10 mmol) was slowly added in portions at −20 °C to the solution of bisketocamphorsulfonylated NOBIN **1–2** (1 mmol) in EtOH (20 ml), respectively, then the reaction mixture was stirred at this temperature for 12 h and quenched by adding 10 ml of saturated ammonium chloride. The mixture was allowed to warm up to room temperature, extracted with EtOAc (3 × 30 ml), washed by brine (30 ml), dried over anhydrous sodium sulfate, and filtered. The filtrate was concentrated in vacuo to give a residue, which was purified by column chromatography (eluting with *n*-hexane/EtOAc = 4/1) to give the titled products correspondingly.

(R_a)-1-[2-({[(1*S*,2*R*,4*R*)-2-hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl]methane}sulfonamido))naphthalen-1-yl])naphthalen-2-yl[(1*S*,2*R*,4*R*)-2-hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl]methanesulfonate (5). Colorless solid (86%); $[\alpha]_D^{30} = -68.2$ (c 0.9, THF); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.15 (d, J = 9.0 Hz, 1H, ArH), 8.09–8.03 (m, 3H, ArH), 7.94 (d, J = 8.1 Hz, 1H, ArH), 7.77 (d, J = 9.0 Hz, 1H, ArH), 7.61–7.57 (t, 1H, ArH), 7.50–7.41 (m, 2H, ArH), 7.36–7.32 (t, 1H, ArH), 7.26 (s, 1H, ArH), 7.10 (d, J = 8.5 Hz, 1H, ArH), 6.47 (s, 1H, NH), 4.04–4.01 (q, 1H, OH), 3.68–3.65 (q, 1H, OH), 3.12 (d, J = 13.7 Hz, 1H, CH_2S), 3.11 (d, J = 13.9 Hz, 1H, CH_2S), 2.77 (d, J = 13.7 Hz, 1H, CH_2S), 2.17 (d, J = 13.9 Hz, 1H, CH_2S), 1.77–0.88 (m, 16H, CH_2, CH), 0.82, 0.78, 0.67, 0.37 (s, 12H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 145.61, 133.88, 133.01, 132.88, 132.50, 131.60, 130.98, 130.54, 128.78, 128.25, 127.57, 127.11, 125.84, 125.77, 125.72, 124.15, 121.86, 121.21, 120.38, 76.23, 75.69, 53.56, 51.86, 50.52, 49.55, 48.71, 48.68, 44.36, 44.23, 39.22, 39.09, 30.42, 29.70, 29.57, 27.27, 27.08, 20.42, 20.07, 19.60, 19.48; ESI-MS calce for $[C_{40}H_{47}NO_7S_2 + Na]^+$ 740.27, found 740.3; *Anal*. Calcd for $C_{40}H_{47}NO_7S_2$: C, 66.92, H, 6.60, N, 1.95, O, 15.60, S, 8.93, Found: C, 66.93, H, 6.33, N, 1.82, O, 15.90, S, 8.98.

(S_a)-1-[2-({[(1*S*,2*R*,4*R*)-2-hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl]methane}sulfonamido))naphthalen-1-yl])naphthalen-2-yl[(1*S*,2*R*,4*R*)-2-hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl]methanesulfonate (6). Colorless solid (88%); $[\alpha]_D^{30} = -18.6$ (c 1.4, THF); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.16 (d, J = 9.0 Hz, 1H, ArH), 8.09–8.03 (m, 3H, ArH), 7.94 (d, J = 8.1 Hz, 1H, ArH), 7.77 (d, J = 9.0 Hz, 1H, ArH), 7.60–7.57 (t, 1H, ArH), 7.50–7.47 (t, 1H, ArH), 7.44–7.40 (t, 1H, ArH), 7.36–7.32 (t, 1H, ArH), 7.25 (d, J = 8.4 Hz, 1H, ArH), 7.09 (d, J = 8.5 Hz, 1H, ArH), 6.44 (s, 1H, NH), 4.01–3.98 (q, 1H, OH), 3.73–3.70 (q, 1H, OH), 3.31 (d, J = 13.7 Hz, 1H, CH_2S), 2.94 (d, J = 13.8 Hz, 1H, CH_2S), 2.45 (d, J = 13.7 Hz, 1H, CH_2S), 2.37 (d, J = 13.8 Hz, 1H, CH_2S), 1.77–1.01 (m, 16H, CH_2, CH), 0.90, 0.71, 0.53, 0.52 (s, 12H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 145.71, 133.72, 132.96, 132.92, 132.47, 131.54, 131.04, 130.63, 128.77, 128.29, 128.24, 127.71, 127.05, 125.98, 125.80, 125.68, 124.19, 121.93, 121.34, 120.21, 76.21, 75.70, 53.22, 51.82, 50.46, 49.65, 48.72, 48.69, 44.31, 44.30, 39.16, 38.99, 30.32, 29.87, 29.70, 27.23, 27.17, 20.19, 19.76, 19.48; ESI-MS calce for $[C_{40}H_{47}NO_7S_2 + Na]^+$ 740.27, found 740.3; *Anal*. Calcd for $C_{40}H_{47}NO_7S_2$: C, 66.92, H, 6.60, N, 1.95, O, 15.60, S, 8.93, Found: C, 66.79, H, 6.52, N, 1.93, O, 15.66, S, 8.90.

Preparation of Mono-N-hydroxycamphorsulfonylated NOBIN 7–8

The general procedure of reduction of **1–2** to give **7–8** is as follows: $NaBH_4$ (10 mmol) was slowly added in portions at −20 °C to the solution of bisketocamphorsulfonylated NOBIN **1–2** (1 mmol) in EtOH (20 ml), respectively. The mixture was stirred at this temperature for 2 h and then continued to stir for 3 h at 25 °C. The mixture was quenched by adding 10 ml of saturated ammonium chloride, extracted with EtOAc (3 × 30 ml), washed by brine (30 ml), dried over anhydrous sodium sulfate, and filtered. The filtrate was concentrated in vacuo to give a residue, which was purified by column chromatography (eluting with *n*-hexane/EtOAc = 4/1) to give the titled products correspondingly.

(R_a)-1-[(1*S*,2*R*,4*R*)-2-hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl]-*N*-[1-(2-hydroxynaphthalen-1-yl)naphthalen-2-yl]methanesulfonamide (7). Colorless solid (80%); $[\alpha]_D^{30} = -76.7$ (c 1.0, THF); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.17 (d, J = 9.0 Hz, 1H, ArH), 8.06–7.93 (m, 4H, ArH), 7.54–7.50 (t, 1H, ArH), 7.43–7.32 (m, 4H, ArH), 7.27 (d, J = 8.6 Hz, 1H, ArH), 7.02 (d, J = 8.3 Hz, 1H, ArH), 6.14 (s, 2H, NH, ArOH), 3.25–3.21 (m, 1H, CHO), 3.17 (d, J = 13.6 Hz, 1H, CH_2S), 2.37 (d, J = 13.6 Hz, 1H, CH_2S), 2.24 (d, J = 3.5 Hz, 1H, OH), 1.61–0.87 (m, 7H, CH_2, CH), 0.81, 0.64 (s, 6H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 152.20, 152.17, 134.20, 133.24, 133.10, 132.05, 132.03, 131.37, 131.07, 129.23, 128.81, 128.51, 128.01, 127.60, 126.16, 125.63, 124.20, 123.34, 118.33, 112.96, 76.47, 52.36, 50.28, 48.65, 44.07, 38.17, 30.39, 27.17, 20.32, 19.52; ESI-MS calce for $[C_{30}H_{31}NO_4S - H]^-$ 500.20, found 500.4; *Anal*. Calcd for $C_{30}H_{31}NO_4S$: C, 71.83, H, 6.23, N, 2.79, O, 12.76, S, 6.39, Found: C, 71.74, H, 6.24, N, 2.68, O, 12.86, S, 6.43.

(S_a)-1-[(1*S*,2*R*,4*R*)-2-hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl]-*N*-[1-(2-hydroxynaphthalen-1-yl)naphthalen-2-yl]methanesulfonamide (8). Colorless solid (87%); $[\alpha]_D^{30} = +10.7$ (c 1.1, THF); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.09–7.93 (m, 5H, ArH), 7.52–7.48 (t, 1H, ArH), 7.43–7.30 (m, 4H, ArH), 7.21 (d, J = 8.5 Hz, 1H, ArH), 7.03 (d, J = 8.4 Hz, 1H, ArH), 6.35 (s, 1H, NH), 5.45 (s, 1H, ArOH), 4.00–3.96 (m, 1H, CHO), 3.25 (d, J = 13.7 Hz, 1H, CH_2S), 2.93 (d, J = 3.8 Hz, 1H, OH), 2.51 (d, J = 13.7 Hz, 1H, CH_2S), 1.78–1.00 (m, 7H, CH_2, CH), 0.90, 0.56(s, 6H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 151.83, 134.44, 133.09, 131.62, 130.90, 129.45, 128.76, 128.44, 127.82, 127.75, 126.03, 125.52, 124.25, 123.87, 120.48, 120.36, 118.10, 112.81, 76.28, 52.64, 50.41, 48.76, 44.29, 38.99, 30.31, 27.22, 26.93, 21.03, 20.22, 19.73; ESI-MS calce for $[C_{30}H_{31}NO_4S - H]^-$ 500.20, found 500.7; *Anal*. Calcd for $C_{30}H_{31}NO_4S$: C, 71.83, H, 6.23, N, 2.79, O, 12.76, S, 6.39, Found: C, 71.96, H, 6.18, N, 2.73, O, 12.88, S, 6.30.

General Procedure for the Catalytic Reactions

Titanium tetraisopropoxide (1.5 mmol) was added via a syringe to the solution of ligands **1–8** (0.1 mmol) in an appropriate freshly dried solvent (3 ml), respectively, and the mixture was stirred for 0.5 h at room temperature. Then, the resulting solution was cooled to 0 °C, dialkylzinc (3 mmol) was added via a syringe, and the mixture was stirred for another 0.5 h at 0 °C, followed by the addition of aldehyde (1 mmol) via a syringe. The reaction mixture was stirred at the same temperature for 0.5–24 h. The mixture was quenched by adding 10 ml of 1 M hydrochloric acid, extracted with EtOAc (3 × 30 ml), washed by brine (30 ml), dried over anhydrous sodium sulfate, and filtered. The filtrate was concentrated in vacuo to give a residue, which was purified by column chromatography (eluting with *n*-hexane/EtOAc) to give the titled secondary alcohol. The ee values of secondary alcohols were analyzed by GC equipped with a Varian CP-Chirasil Dex CB column.

(1*S*)-1-phenylpropan-1-ol. Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.36–7.29 (m, 5H, ArH), 4.56–4.53 (t, 1H, CH), 3.05 (s, 1H, OH), 1.84–1.73 (m, 2H, CH_2), 0.95–0.91 (t, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 144.7, 128.4, 128.1, 127.6, 127.4, 126.4, 126.1, 75.9, 31.9, 10.2; (GC, T = 125 °C): t_R = 9.4 min, t_S = 9.7 min; $[\alpha]_D^{25} = -38.5$ (c 1.0, CCl_3) for 87% ee, {Lit[34] $[\alpha]_D^{20} = -33.5$ (c 2.3, CCl_3) for 86% ee (*S*)}.

(1*S*)-1-(4-chlorophenyl)propan-1-ol. Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.32–7.24 (m, 4H, ArH), 4.55 (t, 1H, CH), 2.38 (s, 1H, OH), 1.80–1.68 (m, 2H, CH_2), 0.92–0.88 (t, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 143.0, 133.0, 128.5, 127.4, 75.2, 31.9, 10.0; (GC, T = 150 °C): t_R = 8.6 min, t_S = 9.1 min; [α] $^{25}_{D}$ = −32.5 (c 1.1, CCl_3) for 85% ee, {Lit[34] [α] $^{20}_{D}$ = −25.5 (c 2.0, CCl_3) for 72% ee (*S*)}.

(1*S*)-1-(4-methoxyphenyl)propan-1-ol. Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.20 (d, J = 8.4 Hz, 2H, ArH), 6.86 (d, J = 8.5 Hz, 2H, ArH), 4.51–4.47 (m, 1H, CH), 3.78 (s, 3H, OCH_3), 2.36 (s, 1H, OH), 1.85–1.63 (m, 2H, CH_2), 0.92–0.88 (t, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 158.9, 134.9, 128.3, 113.6, 79.2, 55.2, 31.3, 10.6; (GC, T = 150 °C): t_R = 8.4 min, t_S = 8.6 min; [α]$^{25}_{D}$ = −30.1 (c 0.9, CCl_3) for 83% ee, {Lit[35] [α]$^{24}_{D}$ = −23.4 (c 0.3, CCl_3) for 65% ee (*S*)}.

(1*S*)-1-[4-(trifluoromethyl)phenyl]propan-1-ol. Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.61 (d, J = 8.2 Hz, 2H, ArH), 7.45 (d, J = 8.2 Hz, 2H, ArH), 4.68–4.65 (t, 1H, CH), 2.33 (s, 1H, OH), 1.85–1.72 (m, 2H, CH_2), 0.95–0.91 (t, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 148.5, 126.2, 125.3, 75.3, 32.0, 9.9; (GC, T = 150 °C): t_R = 4.6 min, t_S = 4.9 min; [α] $^{25}_{D}$ = −19.00 (c 1.00, CCl_3) for 84% ee, {Lit[36] [α] $^{25}_{D}$ = +15.8 (c 1.3, CCl_3) for 72% ee (*R*)}.

(1*S*)-1-(2-methoxyphenyl)propan-1-ol. Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.34 (d, J = 7.5 Hz, 1H, ArH), 7.29–7.25 (t, 1H, ArH), 7.00–6.97 (t, 1H, ArH), 6.90 (d, J = 8.2 Hz, 1H, ArH), 4.85–4.80 (q, 1H, ArCH), 3.86 (s, 3H, OCH_3), 2.82 (d, J = 6.1 Hz, 1H, OH), 1.87–1.80 (m, 2H, CH_2), 1.0–0.97 (t, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 156.5, 132.3, 128.1, 127.0, 120.6, 110.4, 72.2, 55.2, 30.1, 10.4; (GC, T = 150 °C): t_S = 6.5 min, t_R = 7.4 min; [α] $^{25}_{D}$ = −35.5 (c 0.8, CCl_3) for 64% ee, {Lit[36] [α] $^{25}_{D}$ = +40.5 (c 0.45, CCl_3) for 70% ee (*R*)}.

(1*S*)-1-(naphthalen-2-yl)propan-1-ol. Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.89–7.48 (m, 7H, ArH), 4.75–4.72 (t, 1H, CH), 2.64 (s, 1H, OH), 1.97–1.83 (m, 2H, CH_2), 0.99–0.95 (t, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 142.0, 133.3, 133.0, 128.2, 128.0, 127.7, 126.1, 125.8, 124.8, 124.3, 76.1, 31.8, 10.2; (GC, T = 165 °C): t_R = 15.7 min, t_S = 16.2 min; [α] $^{25}_{D}$ = −28.0 (c 0.8, CCl_3) for 78% ee, {Lit[36] [α] $^{25}_{D}$ = +28.6 (c 0.77, CCl_3) for 81% ee (*R*)}.

(1*S*)-1-(naphthalen-1-yl)propan-1-ol. Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.14–7.49 (m, 7H, ArH), 5.36–5.33 (t, 1H, CH), 2.97 (s, 1H, OH), 2.07–1.89 (m, 2H, CH_2), 1.07–1.04 (t, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 140.4, 133.9, 130.6, 129.0, 127.9, 125.9, 125.5, 125.5, 123.4, 123.1, 72.4, 31.2, 10.6; (GC, T = 170 °C): t_S = 12.6 min, t_R = 13.6 min; [α] $^{25}_{D}$ = −40.5 (c 0.9, CCl_3) for 77% ee, {Lit[35] [α] $^{25}_{D}$ = −41.7 (c 0.57, CCl_3) for 78% ee (*S*)}.

(1*S*)-1-(2-methylphenyl)propan-1-ol. Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.49–7.16 (m, 4H, ArH), 4.88–4.85(t, 1H, CH), 2.37 (s, 3H, $ArCH_3$), 2.19 (s, 1H, OH), 1.82–1.75 (m, 2H, CH_2), 1.03–0.99(t, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 142.8, 134.6, 130.3, 127.1, 126.2, 125.3, 72.0, 30.9, 19.1, 10.4; (GC, T = 150 °C): t_R = 5.1 min, t_S = 5.3 min; [α] $^{25}_{D}$ = −12.8(c 0.6, CCl_3) for 22% ee, {Lit[36] [α] $_{D}^{25}$ = +40.5 (c 0.45, CCl_3) for 70% ee (*R*)}.

(1*E*,3*S*)-1-phenylpent-1-en-3-ol. Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.43–7.25 (m, 5H, ArH), 6.59 (d, J = 15.9 Hz, 1H, ArCH), 6.27–6.21 (m, 1H, C = CH), 4.25–4.20 (q, 1H, CH), 1.89 (s, 1H, OH), 1.75–1.62 (m, 2H, CH_2), 1.01–0.97(t, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 136.8, 132.2, 130.4, 128.6, 127.6, 126.5, 74.4, 30.2, 9.8; (GC, T = 130 °C): t_R = 22.0 min, t_S = 22.9 min; [α] $^{25}_{D}$ = −5.0 (c 0.9, CCl_3) for 55% ee, {Lit[35] [α] $^{24}_{D}$ = −5.25 (c 0.45, CCl_3) for 55% ee (*S*)}.

(1*S*)-1-cyclohexylpropan-1-ol. Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 3.24–3.20 (m, 1H, OCH), 2.02 (s, 1H, OH), 1.80–0.94 (m, 13H, CH_2, CH), 0.93–0.89 (t, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 43.1, 29.3, 27.8, 26.7, 26.5, 26.4, 26.2, 10.2; (GC, T = 105 °C): t_S = 16.9 min, t_R = 17.9 min; [α] $^{25}_{D}$ = −8.6 (c 1.1, CCl_3) for 84% ee, {Lit[36] [α] $^{25}_{D}$ = +6.6 (c 0.65, CCl_3) for 68% ee (*R*)}.

(1*S*)-1-phenylethan-1-ol. Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.21–7.10 (m, 5H, ArH), 4.72–4.67 (q, 1H, CH), 2.46 (s, 1H, OH), 1.33 (d, J = 6.5 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 145.9, 128.5, 127.4, 125.5, 70.3, 25.1; (GC, T = 130 °C): t_S = 5.2 min, t_R = 5.0 min; [α] $^{25}_{D}$ = −20.1 (c 1.1, CCl_3) for 44% ee, {Lit[34] [α] $^{20}_{D}$ = −37.5 (c 2.8, CCl_3) for 88% ee (*S*)}.

(1*S*)-1-(2-methylphenyl)ethan-1-ol. Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.55 (d, J = 7.9 Hz, 1H, ArH), 7.30–7.17(m. 3H, ArH), 5.13–5.08 (q, 1H, CH), 2.80 (s, 1H, OH), 2.38(s, 3H, $ArCH_3$), 1.49 (d, J = 6.5 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 144.0, 134.2, 130.3, 127.1, 126.4, 124.6, 66.7, 23.9, 18.9; (GC, T = 130 °C): t_R = 8.9 min, t_S = 10.6 min; [α] $^{25}_{D}$ = −7.2 (c 1.2, CCl_3) for 11% ee, {Lit[34] [α] $^{20}_{D}$ = −35.0 (c 3.4, CCl_3) for 53% ee (*S*)}.

(1*S*)-1-[4-(trifluoromethyl)phenyl]ethan-1-ol. Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.62 (d, J = 8.2 Hz, 2H, ArH), 7.49 (d, J = 8.6 Hz, 2H, ArH), 4.99–4.95(q, 1H, CH), 2.18 (s, 1H, OH), 1.50 (d, J = 6.5 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 149.8, 129.9, 129.5, 125.7, 125.5, 125.4, 122.3, 69.8, 25.4; (GC, T = 145 °C): t_R = 4.3 min, t_S = 4.7 min; [α] $^{25}_{D}$ = −7.2 (c 1.0, CCl_3) for 29% ee, {Lit[34] [α] $^{20}_{D}$ = −29.0 (c 2.0, CCl_3) for 88% ee (*S*)}.

(1*S*)-1-(naphthalen-1-yl)ethan-1-ol. Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.92–7.90 (m, 1H, ArH), 7.72–7.70 (m, 1H, ArH), 7.60 (d, J = 8.2 Hz, 1H, ArH), 7.48 (d, J = 7.1 Hz, 1H, ArH), 7.36–7.27 (m, 3H, ArH), 5.45–5.40 (q, 1H, CH), 2.26 (s, 1H, OH), 1.47 (d, J = 6.5 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 141.5, 133.6, 130.3, 128.9, 127.9, 126.0, 125.6, 123.2, 122.1, 67.0, 24.4; (GC, T = 165 °C): t_S = 13.1 min, t_R = 14.2 min; [α]$^{25}_{D}$ = −23.5 (c 0.9, CCl_3) for 36% ee, {Lit[35] [α] $^{24}_{D}$ = −41.7 (c 0.57, CCl_3) for 78% ee (*S*)}.

RESULTS AND DISCUSSION

Ligand Synthesis

Ligands bisketocamphorsulfonylated NOBIN **1–2** were easily synthesized from the (*R*)-NOBIN and (*S*)-NOBIN by sulfonation with (+)-(*S*)-10-camphorsulfonyl chloride in the presence of triethylamine and a catalytic amount of DMAP at room temperature in excellent yields. The further selective hydrolysis of the sulfonate ester of ligands **1–2** by 3 M NaOH in THF gave corresponding mono-*N*-ketocamphorsulfonylated NOBIN **3–4**. Bishydroxycamphorsulfonylated NOBIN **5–6** were obtained by the reduction of ligands **1–2** using excess of $NaBH_4$ at −20 °C, whereas using excess of $NaBH_4$ at 25 °C resulted in the reduction followed by hydrolysis of ligands **1–2** to give mono-*N*-hydroxycamphorsulfonylated NOBIN **7–8** (Scheme 1). In all cases, the main products of ligands **5–8** are the corresponding exo isomers confirmed by rotating frame Overhauser effect spectroscopy (ROESY) spectroscopic study, which were easily isolated by chromatography on silica gel. The crystal structure of **8** was determined by X-ray diffraction.[37]

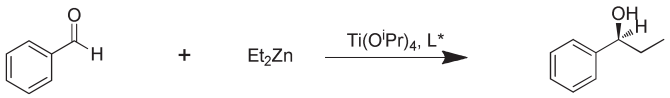
Catalytic Asymmetric Alkylation of Aldehyde with Dialkylzinc

Eight new camphorsulfonylated NOBIN ligands were applied in the asymmetric addition of diethylzinc to benzaldehyde in the presence of titanium tetraisopropoxide, and the results are summarized in Table 1. The data show that both the catalytic activities and enantioselectivities of (*S*)-NOBIN derived

ligands (**2**, **4**, **6**, **8**) were generally better than those of the corresponding (*R*)-NOBIN derivatives (**1**, **3**, **5**, **7**), which should be attributed to the different chiral matching effects of (*R*)-NOBIN and (*S*)-NOBIN's binaphthyl skeleton with (*S*)-camphor's isoborneol backbone. Furthermore, the single sulfonyl derivatives of (*S*)-NOBIN (**4**, **8**) gave better enanotioselectivities than double sulfonyl derivatives (**2**, **6**), which indicated that NOBIN's hydroxyl group improves the performance of the ligands both on the conversion of benzaldehyde and the ee value of the addition product. Compared with ketocamphorsulfonylated NOBIN ligand **4**, the corresponding hydroxycamphorsulfonylated NOBIN ligand **8** gave better enantioselectivity and offered the addition product with opposite configuration possibly because of the use of different spatial arrangement of the complex catalyst. The asymmetric addition of diethylzinc to benzaldehyde catalyzed by ligand **8** could be completed within half an hour in toluene at 0 °C to give (*S*)-1-phenylpropanol with 96% yield and 85% ee value. Next, the influence of the solvent for the asymmetric reaction catalyzed by ligand **8** was examined by performing the reaction in *n*-hexane, toluene, dichloromethane, and THF respectively. The results show that the yields and ee values were higher in reactions carried out in toluene than other solvents (Table 1, entries 8–11). The effect of the sequence of metal addition (Ti/Zn or Zn/Ti) on the addition of diethylzinc to benzaldehyde was also investigated. The result shows that the sequence of adding the metal compounds had no significant effect on the yield and enantiomeric excess (Table 1, entries 8, 12). Finally, by increasing the amount of ligand **8** to 0.3 eq, the ee value of product increased slightly to 87% (Table 1, entriy 13), decreasing the amount of $Ti(O^iPr)_4$ to 0.2 eq, and the yield and ee value of product declined significantly (Table 1, entry 14).

Once the mono-*N*-hydroxycamphorsulfonylated (*S*)-NOBIN, **8** was found to be the best ligand and toluene as the appropriate solvent for the enantioselective addition of diethylzinc to benzaldehyde; other aldehydes were submitted to the enantioselective addition of diethylzinc (Table 2). From the results presented in Table 2, it was found that the position of substituents has significant influence on the enantioselectivity. The orthosubstituted benzaldehydes resulted in the decrease of corresponding ee values (Table 2, entries 6 and 8), which indicates that the catalyst is quite sensitive to steric hindrance. However,

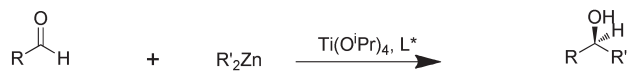
TABLE 1. Chiral ligand-catalyzed additions of diethylzinc to benzaldehyde[a]



				1-Phenylpropan-1-ol.		
Entry	Ligand	Solvent	*t* (h)	Yield[b] (%)	ee[c] (%)	Configuration[d]
1	**1**	Toluene	10	42	4	*R*
2	**2**	Toluene	10	81	7	*R*
3	**3**	Toluene	10	50	7	*S*
4	**4**	Toluene	2	94	64	*R*
5	**5**	Toluene	10	50	11	*R*
6	**6**	Toluene	10	48	77	*S*
7	**7**	Toluene	5	70	30	*R*
8	**8**	Toluene	0.5	96	85	*S*
9	**8**	THF	24	0	—	—
10	**8**	DCM	10	30	40	*S*
11	**8**	*n*-Hexane	24	0	—	—
12[e]	**8**	Toluene	1	95	85	*S*
13[f]	**8**	Toluene	1	95	87	*S*
14[g]	**8**	Toluene	24	30	40	*S*

[a]Reaction conditions: 1 mmol of benzaldehyde, 0.1 mmol of ligand, 1.5 mmol of $Ti(O^iPr)_4$, 3 mmol of Et_2Zn, and in 3 ml of solvent.
[b]Isolated yields.
[c]Determined by gas chromatography analysis using a Varian CP-Chirasil Dex CB column.
[d]The configuration was determined by comparing the sign of specific rotation value with the literature value[34].
[e]Firstly, diethylzinc was added and then stirred for 0.5 h at 0 °C, followed by the addition of titanium tetraisopropoxide.
[f]0.3 mmol of ligand was used.
[g]0.2 mmol of $Ti(O^iPr)_4$ was used.

TABLE 2. Enantioselective additions of dialkylzinc reagents to aldehydes catalyzed by titanium complex of ligand 8[a]



Entry	RCHO	R′$_2$Zn	Yield[b] (%)	ee[c] (%)	Configuration[d]
1	4–ClC_6H_4CHO	Et_2Zn	98	85	*S*
2	4–$CH_3OC_6H_4CHO$	Et_2Zn	96	83	*S*
3	4–$CF_3C_6H_4CHO$	Et_2Zn	95	84	*S*
4	2–Naphthaldehyde	Et_2Zn	93	78	*S*
5	1–Naphthaldehyde	Et_2Zn	90	77	*S*
6	2–$CH_3C_6H_4CHO$	Et_2Zn	96	22	*S*
7	(*E*)–PhCHCHCHO	Et_2Zn	75	55	*S*
8	2–$CH_3OC_6H_4CHO$	Et_2Zn	97	64	*S*
9	cyclohexanecarbaldehyde	Et_2Zn	90	84	*S*
10	PhCHO	Me_2Zn	95	44	*S*
11[e]	PhCHO	Me_2Zn	98	31	*S*
12	2–$CH_3C_6H_4CHO$	Me_2Zn	98	11	*S*
13	1–Naphthaldehyde	Me_2Zn	97	36	*S*
14	4–$CF_3C_6H_4CHO$	Me_2Zn	97	29	*S*

[a]Reaction conditions: 1 mmol of aldehyde, 0.1 mmol of ligand **8**, 1.5 mmol of $Ti(O^iPr)_4$, 3 mmol of R′$_2$Zn, and in 3 ml of solvent.
[b]Isolated yields.
[c]Determined by gas chromatography analysis using a Varian CP-Chirasil Dex CB column.
[d]The configuration was determined by comparing the sign of specific rotation value with the literature value[34–36].
[e]Reaction temperature: −15 °C.

the electronic effect of substituents on the reaction yield and enantioselectivity is not obvious (Table 2, entries 1, 2, 3, and 9). Instead of diethylzinc, dimethylzinc gave significantly declined ee values of the addition products (Table 2, entries 10–14).

Possible Catalytic Transition State and Mechanism

Detailed studies on catalytic reaction mechanism of the asymmetric additions of dialkylzinc reagents to aldehydes and ketones in the presence of a chiral ligand and $Ti(O^iPr)_4$ have shown that the possible structure for the catalyst is a bimetallic titanium complex.[28,32,38,39] To investigate if the enantioselective addition of dialkylzinc reagents to aldehydes catalyzed by our ligand **8** is also governed by this mechanism or not, a titration of ligand **8** with $Ti(O^iPr)_4$ was undertaken. Thus, to a $CDCl_3$ or D_8-toluene solution of ligand **8** (150 mM), 0.5 and 15 eq amounts of $Ti(O^iPr)_4$ were added, respectively, and the ^1H NMR and ^{13}C NMR spectra of the resulting solutions were recorded accordingly.

As shown in Figures 1 and 2, we identified two ligand **8**-titanium complexes I and II by comparing our titration data. At low titanium/ligand **8** ratios, complex I, recognized as a 1:1 mononuclear $TiL^*(O^iPr)_2$ ($L^* = \mathbf{8}$)complex, was dominant (Figs. 1B and 2B), whereas complex II, recognized as a 2:1 dinuclear $Ti_2L^*(O^iPr)_5$ complex, was dominant in the presence of 15 eq of $Ti(O^iPr)_4$ (Figs. 1C and 2C) because of the equilibrium shifting from I to II driven by excess $Ti(O^iPr)_4$, which was also observed previously for 1,1′-bi-2-naphthol-based ligands[40,41] and Sharpless' tartrate esters.[42] The aromatic proton signals and aromatic ipsocarbon signals for both species I and II were shifted to downfield with respect to free ligand **8** as a consequence of titanium complexation by oxygen or nitrogen donor ligands.[43,44] An important resonance at 87.6 ppm of ^{13}C NMR spectrum, which belongs to the tertiary carbon of complex II's bridging isopropoxy (the tertiary carbon signal of $Ti(O^iPr)_4$ at 76.2, the tertiary carbon signal of isopropanol at 64),[40] was observed (Fig. 2C). Therefore, the possible catalyst structure of ligand **8**-catalyzed asymmetric addition of dialkylzincs to aldehydes is dinucear titanium. From the results presented in Table 1, entries 14 and 8, it was found that the more complex II the solution has, the higher yield and enantioselectivity the reaction has. That means that complex II has better catalytic activity and enantioselectivity than complex I.

The transition state of ligand **8**-titanium complex II-catalyzed asymmetry addition of dialkylzincs to aldehydes was proposed as shown in Figure 3. Aldehyde approaches the top titanium in a way that the aldehyde's *R* group is pointing toward the other side of the bridging oxygen donor of

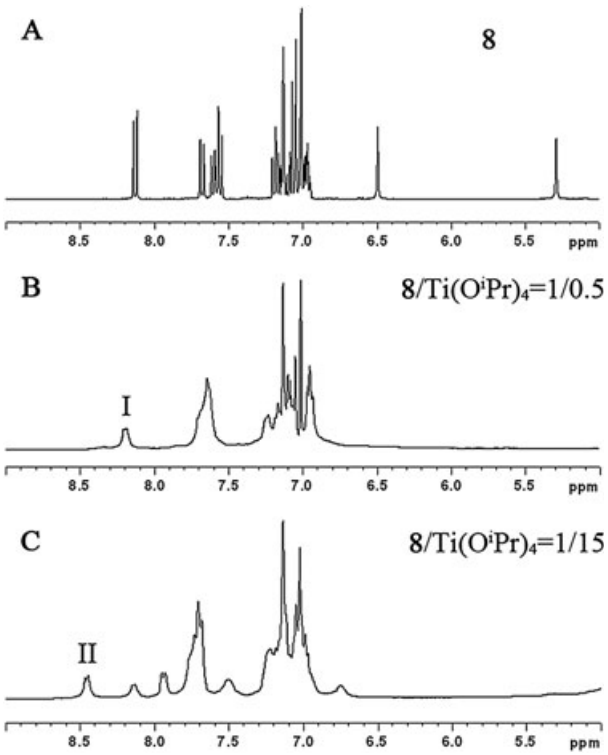


Fig. 1. ^1H nuclear magnetic resonance spectra in D_8-toluene at room temperature of **8**/$Ti(O^iPr)_4$ at different ratios.

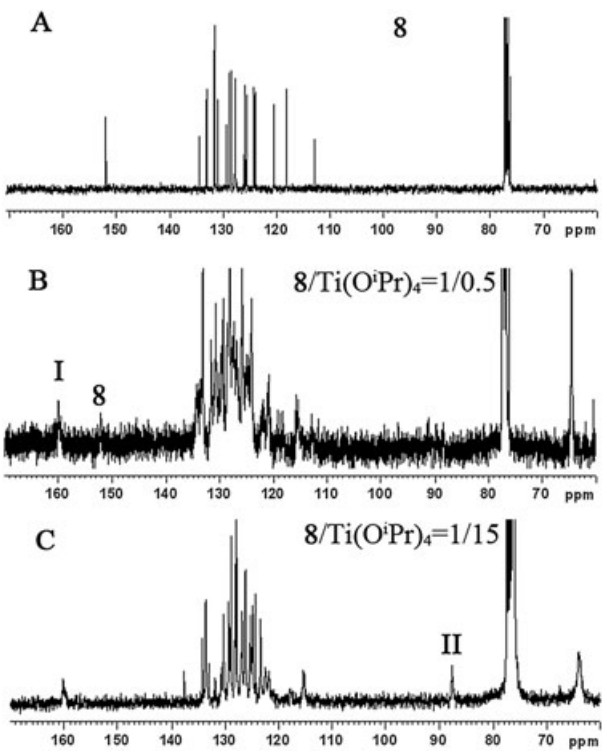


Fig. 2. ^{13}C nuclear magnetic resonance spectra in $CDCl_3$ at room temperature of **8**/$Ti(O^iPr)_4$ at different ratios.

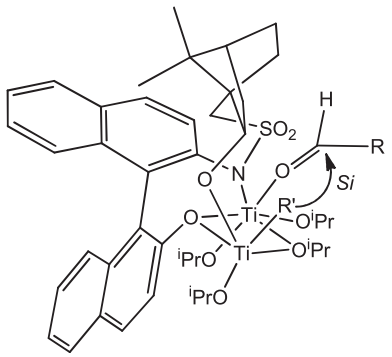


Fig. 3. Proposed transition state for ligand **8**-titanium complex II-catalyzed asymmetry addition of dialkylzincs to aldehydes.

NOBIN because the steric effect of bulky camphor moiety causes positioning of the aldehyde's *R* group away from the camphor moiety. Then, the alkyl group coming from dialkylzinc and attaching to the bottom titanium attacks the carbonyl carbon of aldehyde from *Si* face to obtain the (*S*)-addition product.

CONCLUSIONS

In conclusion, we have synthesized a series of new camphorsulfonylated ligands derived from both (*R*)-NOBIN and (*S*)-NOBIN and assessed their enantioselectivities in the addition of dialkylzinc reagents to aldehydes in the presence of titanium tetraisopropoxide. The highest catalytic efficiency was obtained with mono-*N*-hydroxycamphorsulfonylated (*S*)-NOBIN **8** in toluene, which gave (*S*)-addition products with high yields and ee values up to 87%. On the basis of the ^{1}H NMR and ^{13}C NMR spectroscopic studies on the possible catalyst structure, a binuclear titanium complex is proposed, and a catalytic mechanistic explanation is also provided.

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