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A facile synthesis and asymmetric catalytic activity of new 3-substituted chiral BINOL ligands

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Three new chiral ligands, (*S*)-3-(1H-imidazol-1-yl)methyl-1,1′-binaphthol [(*S*)-1], (*S*)-3-(1H-1,2,3-benzotriazol-1-yl)methyl-1,1′-binaphthol [(*S*)-2] and (*S*)-3-(2H-1,2,3-benzotriazol-2-yl)methyl-1,1′-binaphthol [(*S*)-3], were prepared by a simple method. They showed moderate catalytic properties for the asymmetric addition of diethylzinc to benzaldehyde in the presence of titanium tetraisopropoxide. Copyright © 2008 John Wiley & Sons, Ltd.

Keywords: BINOL; 1,2,3-benzotriazole; imidazole; diethylzinc; asymmetric addiotion

Introduction

After the structure of (*R*)-1,1′-binaphthol (BINOL) was determined by X-ray diffraction in 1971,[1] many substituted BINOL ligands were designed and synthesized. Substituents at the 3-position of BINOL are normally introduced via a two-step protocol that involves treatment of a suitably protected BINOL with an organolithium reagent, followed by reaction with an electrophile. Lingenfelter *et al*.[2] synthesized two enantiomerically pure 3,3′-diaryl BINOLs by Grignard cross-coupling reaction of 3,3′-dibromo-2,2′-dimethyl-BINOL and arylmagnesium bromides. Cox *et al*. reported an expedient synthetic route to 3 or 3,3′-substituted-1,1′-binaphthols by directed *ortho*-metallation and Suzuki cross-coupling methods.[3] BINOL ligands substituted by the introduction of heteroaromatic groups at the 3 or 3,3′-positions are less reported. Simonsen *et al*. reported the synthesis of 3,3′-diaryl-BINOLs by reaction of 2,2′-dimethoxy-1,1′-binaphthyl-3,3′-diyldiboronic acid with aryl bromides using the Suzuki cross-coupling reaction.[4] Jin *et al*. synthesized 3,3′-dipyridyl BINOLs by Suzuki coupling.[5] Recently, Matsui *et al*. reported the synthesis of BINOLs 3-substituted by various pyridyls or pyridinylaminomethyls.[6] In our previous research, 1,3,5-triazin-2-yl or 2-quinolyl were respectively introduced to the 3 or 3,3′-positions of BINOL.[7]

Herein, we report the synthesis of new chiral ligands (*S*)-3-(1H-imidazol-1-yl)methyl-1,1′-binaphthol [(*S*)-**1**], (*S*)-3-(1H-1,2,3-benzotriazol-1-yl)methyl-1,1′-binaphthol [(*S*)-**2**] and (*S*)-3-(2H-1,2,3-benzotriazol-2-yl)methyl-1,1′-binaphthol [(*S*)-**3**] and their application in the asymmetric addition of diethylzinc to aldehydes.

Results and Discussion

Synthesis of the new 3-substituted chiral BINOL ligands

The three new 3-substituted chiral BINOL ligands were prepared as shown in Scheme 1. At first intermediate (*S*)-3-(methanesulfonato)methyl-2,2′-dimethoxylmethyl-1,1′-binaphthol [(*S*)-**6**] was synthesized from (*S*)-2,2′-dimethoxylmethyl-1,1′-binaphthol [(*S*)-**4**] through four steps according to the literature.[8] After the reaction of (*S*)-**6** with imidazole, new intermediate (*S*)-3-(1H-imidazol-1-yl)methyl-2,2′-dimethoxylmethyl-1,1′-binaphthol [(*S*)-**7**] was obtained. However, after the reaction of (*S*)-**6** with 1,2,3-benzotriazole, two new intermediates (*S*)-3-(1H-1,2,3-benzotriazol-1-yl)methyl-2,2′-dimethoxylmethyl-1,1′-binaphthol [(*S*)-**8**] and (*S*)-3-(2H-1,2,3-benzotriazol-2-yl)methyl-2,2′-dimethoxylmethyl-1,1′-binaphthol [(*S*)-**9**] were obtained in approximately equal yields. Although the ^{1}H and ^{13}C NMR spectra of (*S*)-**9** were different from that of (*S*)-**8**, their molecular weights determined by HRMS were the same. The colorless crystals of (*S*)-**8** and (*S*)-**9** were obtained from their diethyl ether solutions, respectively. The crystal structures of (*S*)-**8**[9] and (*S*)-**9**[10] were determined by X-ray diffraction, as shown in Fig. 1. It was obvious that the 3-methylene of (*S*)-**8** was connected with N(1) of 1,2,3-benzotriazole while that of (*S*)-**9** was connected with N(2) of 1,2,3-benzotriazole.

1,2,3-Benzotriazole might exist as 1H-configuration and 2H-configuration (Fig. 2).[11] When it reacted with the electrophilic reagent, the two configurations competed with each other. As a result, the two products could be obtained. After deprotection, the target compounds (*S*)-**1,** (*S*)-**2** and (*S*)-**3** were obtained from their corresponding precursors (*S*)-**7,** (*S*)-**8** and (*S*)-**9**, respectively.

Asymmetric addition of diethylzinc to aldehydes

The effectiveness of the three ligands in the titanium complex-catalyzed enantioselective addition of diethylzinc to benzaldehyde

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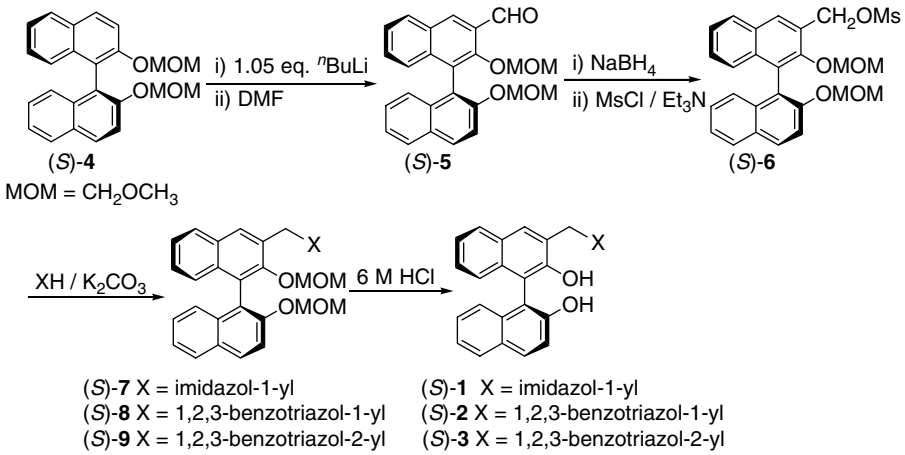

Scheme 1. Synthesis of chiral 3-substituted BINOL ligands.

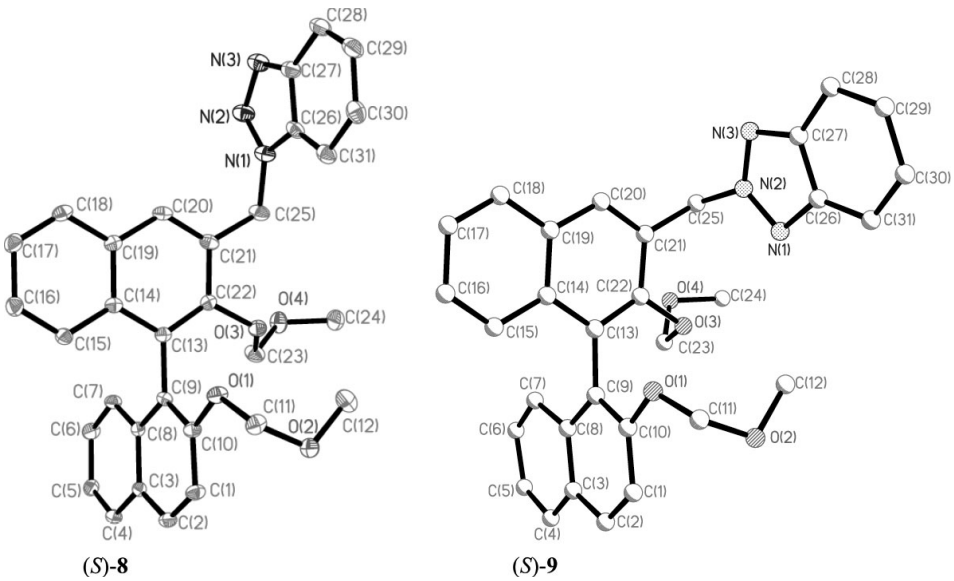

Figure 1. Molecular structure and atomic numbering scheme of (S)-3-(1H-benzotriazo-1-yl)methyl-2,2,-dimethoxymethyl-1,1,-binaphthol [(s)-8] and (S)-3-(1H-benzotriazo-2-yl)methyl-2,2,-dimethoxymethyl-1,1,-binaphthol [(s)-9].

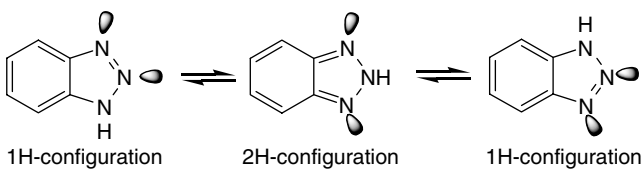

Figure 2. 1H-Configuration and 2H-configuration of 1,2,3-benzotriazole.

was tested.[12] The active catalyst was formed *in situ* by mixing the ligand with titanium tetraisopropoxide in toluene.[13] In this reaction, the molar ratio of ligand:Ti(O^iPr)$_4$: Et_2Zn:benzaldehyde was set up to be 0.1 : 1.2 : 3:1. (*S*)-**1**, (*S*)-**2** and (*S*)-**3** showed moderate catalytic properties and (*S*)-**3** gave the best result (entry 3, 77.5% ee). The results are summarized in Table 1.

In conclusion, we synthesized three new chiral ligands (*S*)-**1**, (*S*)-**2** and (*S*)-**3**, and used them in asymmetric addition of diethylzinc to benzaldehyde to give secondary alcohols in high yields and moderate ee values.

Experimental

Materials

All experiments that were sensitive to moisture or air were carried out under an argon atmosphere using standard Schlenk techniques. Diethylzinc (1.94 M in hexane) was purchased from Aldrich. All anhydrous solvents were purified and dried by standard techniques just before use.

NMR analyses

The ^1H and ^{13}C NMR spectra were recorded on a Bruker AC-300 instrument in $CDCl_3$ solution with TMS as internal standard.

Elemental analyses and HRMS studies

The high-resolution mass spectra (MALDI-HRMS) were measured on an Ionspec FT MS 7.0 T spectrometer. Elemental analysis was performed with a Yanaco CHN Corder MT-3 elemental analyzer.

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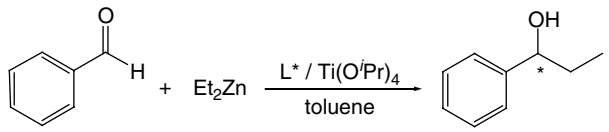
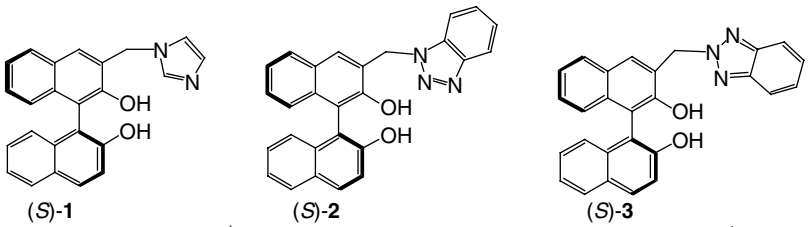
Table 1. Catalytic asymmetric addition of diethylzinc (2.56 M in hexane) to benzaldehyde





(*S*)-**1** (*S*)-**2** (*S*)-**3**

Entry	L* (mol %)	L* : Ti(O^{i}Pr)$_4$ (M/M)	Yield (%)[a]	ee (%)[b]	Configuration[c]
1	(*S*)-**1** (10)	1 : 12	86.5	53.1	*S*
2	(*S*)-**2** (10)	1 : 12	86.7	63.1	*S*
3	(*S*)-**3** (10)	1 : 12	90.6	77.5	*S*

[a] Isolated yield.
[b] Data were determined by GC analysis using a chiral column (chiral beta-DEX 120 capillary column).
[c] Based on the reported optical rotation (Dai *et al.*[14])

Chiral chromatography analyses

Optical rotations analyses

Optical rotations were measured on a Perkin-Elmer 241 polarimeter.

Ee value analyses

Ee values of the product in asymmetric reaction were determined by GC analysis using a chiral column. Gas chromatography analyses were performed on a chiral beta-DEX 120 capillary column.

X-ray crystallography

The X-ray crystallography data of the two chiral compounds (*S*)-**8** and (*S*)-**9** were determined using a Bruker smart Apex ii X-ray crystallographic instrument.

Synthesis of the intermediates

(*S*)-**7**, (*S*)-**8** and (*S*)-**9** were synthesized by similar procedures. The obtained (*S*)-3-(methanesulfonato)methyl-2,2′-dimethoxylmethyl-1,1′-binaphthol (*S*)-**6** (2.02 g, 4.2 mmol) was dissolved in 100 ml acetone. 1H-imidazole (0.30 g, 4.4 mmol) and anhydrous K_2CO_3 (0.61 g, 4.4 mmol) were added successively. The reaction mixture was refluxed for 7 h. The precipitate was filtered off and the solvent was removed under reduced pressure. The residue was chromatographed (hexane : ethyl acetate = 1 : 1) to afford compound (*S*)-**7** (1.09 g, 2.4 mmol) in 57% yield as a yellow semi-solid. $[\alpha]_D^{25} = -67.1$ (c 3.3, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.98 (d, J = 9.07 Hz, 1H), 7.89 (d, J = 8.11 Hz, 1H), 7.78 (d, J = 8.20 Hz, 1H), 7.74 (s, 1H), 7.60 (d, J = 9.09 Hz, 1H), 7.48 (s, 1H), 7.35–7.41 (m, 2H), 7.27–7.31 (m, 1H), 7.21–7.24 (m, 1H), 7.11–7.18 (m, 4H), 5.49 (dd, J = 19.63 Hz, 2H), 5.08 (dd, J = 19.19 Hz, 2H), 4.53 (d, J = 5.77 Hz, 1H), 4.44 (d, J = 5.77 Hz, 1H), 3.17 (s, 3H), 3.11 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 152.86, 151.93, 137.75, 133.84, 133.75,, 130.74, 130.22, 130.02, 129.66, 129.34, 128.04, 127.93, 127.84, 126.95, 126.65, 125.71, 125.61, 125.44, 125.20, 124.27, 119.89, 119.71, 116.32, 99.48, 94.83, 57.02, 56.00, 47.11. MALDI-TOF-HRMS Calcd for $C_{28}H_{26}N_2O_4$ (M^+ 454.1959); found: 455.1965 $[M + H]^+$.

(*S*)-**8** white solid, yield 41.7%. m.p. 120–121 °C. $[\alpha]_D^{25} = -86.3$ (c 0.2, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.12 (d, J = 8.06 Hz, 1H), 7.99 (d, J = 9.05 Hz, 1H), 7.89 (d, J = 8.16 Hz, 1H), 7.68 (d, J = 8.13 Hz, 1H), 7.58–7.61 (m, 2H), 7.52 (s, 1H), 7.28–7.44 (m, 4H), 7.10–7.23 (m, 4H), 6.25 (q, J = 8.44 Hz, 2H), 5.04 (dd, J = 6.92 Hz, 2H), 4.62 (dd, J = 5.86 Hz, 2H), 3.19 (s, 3H), 3.11 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 152.85, 151.93, 146.35, 133.83, 133.77, 130.73, 130.22, 129.68, 128.45, 128.40, 128.03, 127.31, 126.89, 126.66, 125.69, 125.39, 125.29, 124.28, 123.92, 119.99, 118.23, 116.33, 110.21, 99.78, 94.81, 57.25, 55.94, 47.91. Anal. calcd for $C_{31}H_{27}N_3O_4$ (M_r = 505.2): C, 73.65; H, 5.38; N, 8.31. Found: C, 73.75; H, 5.26, N, 8.50.

(*S*)-**9** white solid, yield 40.1%. m.p. 154–156 °C. $[\alpha]_D^{25} = -41.4$ (c 0.02, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.86–7.99 (m, 4H), 7.74–7.77 (d, J = 8.45 Hz, 1H), 7.57–7.60 (m, 2H), 7.34–7.44 (m, 5H), 7.18–7.21 (m, 3H), 6.30 (s, 2H), 5.07 (q, J = 6.85 Hz, 2H), 4.60 (dd, J = 5.52 Hz, 2H), 3.14 (s, 3H), 3.07 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 156.37, 155.10, 152.90, 144.70, 133.95, 133.88, 130.74, 130.07, 128.75, 128.12, 127.92, 126.85, 126.57, 126.35, 125.70, 125.62, 125.48, 124.20, 124.20, 120.19, 118.23, 116.46, 116.33, 99.55, 94.80, 57.01, 56.35, 55.97. MALDI-TOF-HRMS calcd for $C_{31}H_{27}N_3O_4$ (M^+ 505.2074); found: 506.2077 $[M + H]^+$.

Synthesis of the products

(*S*)-**1**, (*S*)-**2** and (*S*)-**3** were synthesized by similar procedures. (*S*)-**7** (1.14 g, 2.5 mmol) was dissolved in the mixed solvent of methanol–dichloromethane (30/30 ml). At 0 °C HCl (6 M, 1.6 ml) was added dropwise. The reaction mixture was stirred at room temperature for 3 h and the solvent was removed under reduced pressure. The residue was extracted with ethyl acetate (50 ml). The extract was washed with water, saturated $NaHCO_3$ and brine in turn. After drying over Na_2SO_4 and removal of solvent, compound (*S*)-**1** (0.84 g, 2.3 mmol) was obtained in 92% yield as a white solid,

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m.p. 134–136 °C. $[\alpha]_D^{25} = -16.9$ (c 0.7, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.92 (d, $J = 8.93$ Hz, 1H), 7.85 (t, $J = 7.48$ Hz, 3H), 7.55 (s, 1H), 7.40 (d, $J = 8.92$ Hz,, 2H), 7.33 (m, 2H), 7.26 (m, 1H), 7.20 (t, $J = 8.76$ Hz 2H), 7.05 (d, $J = 8.40$ Hz 1H), 6.94 (s, 1H), 5.55 (dd, $J = 15.14$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 153.77, 150.34, 136.82, 133.80, 131.34, 129.47, 129.25, 128.94, 128.36, 128.12, 127.69, 127.53, 127.25, 125.00, 124.74, 124.37, 124.11, 124.06, 123.69, 120.62, 119.47, 118.71, 110.79, 46.89. MALDI-TOF-HRMS calcd for $C_{24}H_{19}N_2O_2$ (M^+ 366.1436); found: 367.1441 $[M + H]^+$.

(*S*)-**2** white solid, yield 86.6%. m.p. 136–138 °C. $[\alpha]_D^{25} = -37.8$ (c 0.3, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.09 (d, $J = 8.14$ Hz, 1H), 7.99 (d, $J = 8.96$ Hz, 1H), 7.91 (d, $J = 8.03$ Hz, 1H), 7.72–7.77 (m, 2H), 7.63 (d, $J = 8.08$ Hz, 1H), 7.32–7.47 (m, 7H), 7.07–7.14 (m, 2H), 6.12 (s, 1H), 5.44 (s, 1H), 5.12 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 152.96, 150.24, 146.04, 133.28, 133.18, 131.93, 131.71, 130.58, 129.49, 129.08, 128.50, 127.90, 127.67, 127.62, 127.50, 127.45, 124.61, 124.16, 124.02, 123.98, 123.64, 120.01, 117.97, 112.13, 110.34, 109.94, 47.15. MALDI-TOF-HRMS Calcd for $C_{27}H_{19}N_3O_2$ (M^+ 417.1512); found: 418.1547 $[M + H]^+$.

(*S*)-**3** white solid, yield 89.2%. m.p. 114–116 °C. $[\alpha]_D^{25} = -40.5$ (c 0.04, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.81–7.97 (m, 6H), 7.27–7.42 (m, 7H), 7.20–7.17 (m, 2H), 6.17 (q, $J = 8.08$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 151.49, 150.10, 143.50, 132.94, 132.44, 130.41, 130.29, 128.48, 128.16, 127.62, 127.48, 127.01, 126.37, 125.80, 125.65, 123.65, 123.49, 123.43 122.97, 122.78, 117.19, 116.87, 112.48, 110.75, 99.11, 99.06, 55.50. MALDI-TOF-HRMS calcd for $C_{27}H_{19}N_3O_2$ (M^+ 417.1512); found: 418.1569 $[M + H]^+$.

A typical procedure for the asymmetric addition of diethylzinc to aldehyde

Titanium tetraisopropoxide (0.21 ml, 0.7 mmol) was added to a solution of (*S*)-**1** (0.02 g, 0.05 mmol) in 3 ml toluene at room temperature and the reaction mixture was stirred for 30 min followed by the addition of diethylzinc (2.59 M in hexane, 1.16 ml) with continued stirring for 15 min. The solution was cooled to 0 °C and benzaldehyde (0.106 g, 1 mmol) was added. The reaction mixture was filtered to remove the insoluble material and the filtrate was extracted with 3 × 20 ml toluene. The combined organic layers were dried over $MgSO_4$ and concentrated until solvent free. The residue was purified by column chromatography on silica gel affording 1- phenyl-1-propanol as a light yellow liquid. The enantiomeric excess of the products was determined by GC on a Chiral beta-DEX 120 capillary column.

Acknowledgments

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Supplementary Data

The crystallographic data of the chiral ligands (*S*)-**8** and (*S*)-**9** have been deposited with the Cambridge Crystallographic Data Centre as CCDC number 651946 and 651947 respectively. Copies of the data can be obtained on request to CCDC, 12 Union Road, Cambridge CB21 EZ, UK, e-mail: deposited@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk.

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[10] Crystallographic data for chiral intermediate (*S*)-**9**, $C_{32}H_{27}NO_3$, formula weight 505.56, monoclinic, P-1, $a = 10.3844(14)$ Å, $b = 8.1233(9)$ Å, $c = 15.320(2)$ Å, $\alpha = 90°$, $\beta = 108.967(5)°$, $\gamma = 90°$, $V = 1222.1(3)$ Å^3, $Z = 2$, $D_{calcd} = 1.374$ g cm^{-3}, $T = 113(2)$ *K*, μ (Mo Kα) = 0.092 mm^{-1}, *R*1 (*wR*2) = 0.0759 (0.1662), crystal dimensions 0.10 × 0.08 × 0.08 mm. (CCDC 651947).
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