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Titanium (IV) as an essential promoter in the asymmetric addition of diethylzinc to aldehydes catalyzed by aminonaphthol and imine ligands based on 3-substituted binaphthol

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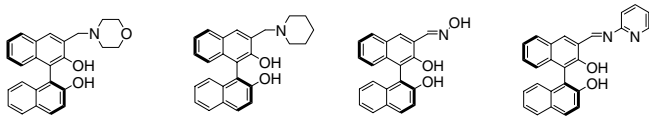
Abstract

By using indirect reductive amination and condensation, two types of aminonaphthol and imine ligands based on 3-substituted binaphthol have been synthesized, respectively. When their catalytic effectiveness was tested by the ethylation of aldehydes with diethylzinc, titanium tetraisopropoxide was found essential to get good results with ee up to 90%.

Keywords: Reductive amination; BINOL; Diethylzinc; Titanium tetraisopropoxide

1. Introduction

Over the past decades, the enantioselective alkylation of carbonyl compounds has been dramatically improved, owing to the use of organozinc reagents in the presence of a wide variety of chiral auxiliaries [1]. And a large number of chiral catalysts such as β-amino alcohols (particularly those possessing a tertiary amino group) [2], amino thiols [3], aminonaphthols [4], imines [5] and titanium complexes [6] have been developed and high enantioselectivities have been achieved. Thus, the reaction of diethylzinc with aldehydes has become a classical test in the design of new ligands for catalytic asymmetric synthesis. Despite the enormous success of axially chiral ligands in asymmetric reactions, a limited number of aminonaphthol [7] and imine [8] type ligands based on BINOL are reported for diethylzinc addition to aldehydes. To the best of our knowledge, there have never been such type ligands prepared from 3-formyl BINOL [9] in the long catalyst list of the asymmetric addition of diethylzinc to aldehydes. Therefore, it should be of interest to explore the catalytic ability of the aminonaphthol and imine ligands with a scaffold of 3-substituted BINOL. In this paper, we report the synthesis of chiral aminonaphthol ligands (*S*)-**1** and (*S*)-**2** as well as imine ligands (*S*)-**3** and (*S*)-**4**, together with their catalytic applicability in the addition of diethylzinc to aldehydes.



(*S*)-**1** (*S*)-**2** (*S*)-**3** (*S*)-**4**

Among the four ligands, (*S*)-**1** is a known compound synthesized as a byproduct in a short but severe Mannich-type procedure with partial racemization [10]. Here (*S*)-**1** is synthesized under mild reaction condition in high yield without racemization.

2. Results and discussion

(*S*)-**1** and (*S*)-**2** were easily prepared in high yield by indirect reductive amination of (*S*)-**3**-formyl BIONL with

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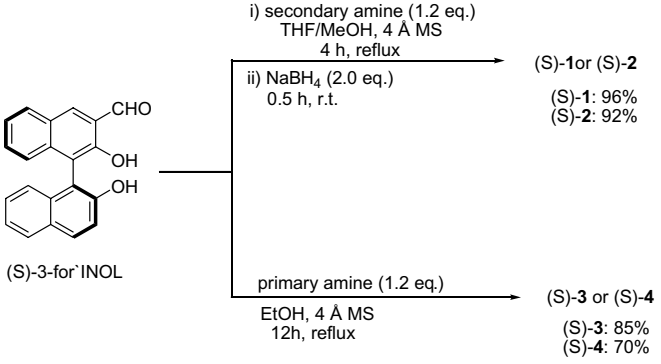
morpholine and piperidine in the presence of $NaBH_4$, respectively [11]. (*S*)-**3** and (*S*)-**4** were also conveniently prepared from condensation of (*S*)-**3**-formyl BINOL with hydroxylamine hydrochloride and 2-aminopyridine in good yield (Scheme 1) [12].

A pale yellow single crystal of *rac*-**3** · THF was obtained from THF-petroleum ether solution. The crystal structure was determined by X-ray diffraction as shown in Fig. 1 [13]. The oxime has a *trans* configuration. The torsion angle of C(20)–C(19)–C(21)–N(1) is 2.1°, and the dihedral angle between the two naphthalene systems is 82.3°.

First, the effectiveness of the four ligands as chiral catalysts for the ethylation of aldehydes with Et_2Zn was tested. The addition reaction was carried out in toluene at room temperature. Unfortunately, neither the chemical yields nor the enantioselectivities were satisfactory (Table 1). Ligand (*S*)-**3** (5 mol%) only gave a 67% yield and 32% ee as the best result (Entry 3). In addition, the reduced benzyl alcohol products were also observed in about 15% yield for (*S*)-**1** and (*S*)-**2** (Entry 1 and 2).

Titanium (IV) complexes with various chiral ligands have been extensively confirmed as an effective promoter for the asymmetric addition of diethylzinc to aldehydes in the last years. Hence, aimed at improving the catalytic performance of the four ligands (*S*)-**1**–**4**, $Ti(O^iPr)_4$ was added



Scheme 1. Synthesis of (*S*)-**1**–**4**.

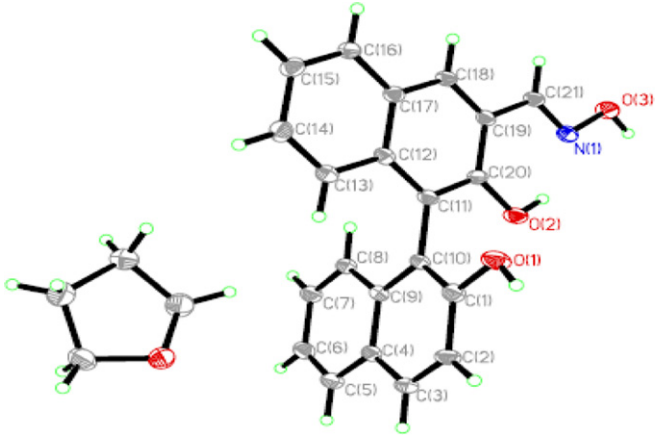
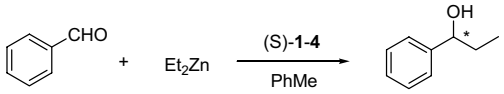


Fig. 1. The molecular structure of **3** including one THF molecule.

Table 1
Catalytic asymmetric addition of diethylzinc (1.5 M in hexane) to benzaldehyde using ligands (*S*)-**1**–**4**



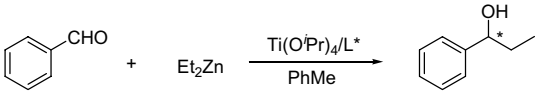
Entry	Ligand (mol%)[a]	Yield (%)[b]	ee (%)[c]	Config.[d]
1	(*S*)-**1** (10)	51 (13)	13	*S*
2	(*S*)-**2** (10)	38 (16)	16	*S*
3	(*S*)-**3** (5)	67	32	*S*
4	(*S*)-**4** (5)	57	15	*S*

[a] Et_2Zn/benzaldehyde = 3:1; reaction temperature: r.t.; reaction time: 48 h.
[b] Isolated yield and the data in brackets refers to the amount of benzyl alcohol product.
[c] Data were determined by GC analysis using a chiral column (Chiral beta-DEX 120 capillary column).
[d] The absolute configuration of the products were determined by comparison to the literature data.

and it resulted in a dramatic enhancement not only in chemical yields but in ee values (Table 2). Again, (*S*)-**3** (20 mol%) gave the best result with a 93% yield and 89% ee in the presence of 1.2 equiv. $Ti(O^iPr)_4$ (Entry 4). Furthermore, the reduced benzyl alcohol products were not detected at all for (*S*)-**1** and (*S*)-**2** (Entry 1–3).

With conditions optimized for benzaldehyde, the use of ligand (*S*)-**3** was extended to the asymmetric ethylation of other aromatic and α,β-unsaturated aldehydes (Table 3). The additions were completed within 5 h at room temperature with good yields and ee values for all the aldehydes. For anisaldehyde possessing an electron-donating group in *para* position and *trans*-cinnamaldehyde, a slight decreased enantioselectivity was observed (Entry 4 and 6). The best enantioselectivities up to 90% ee were obtained with *p*-bromobenzaldehyde and *o*-methoxybenzaldehyde (Entry 3 and 5).

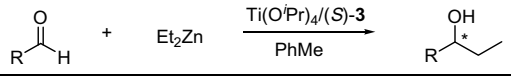
Table 2
Addition of diethylzinc (1.5 M in hexane) to benzaldehyde using ligands (*S*)-**1**–**4** in the presence of titanium tetraisopropoxide



Entry	Ligand (mol%)[a]	Yield (%)[b]	ee (%)[c]	Config.[d]
1	(*S*)-**1** (20)	85	76	*S*
2	(*S*)-**1** (10)	83	72	*S*
3	(*S*)-**2** (10)	80	56	*S*
4	(*S*)-**3** (20)	93	89	*S*
5	(*S*)-**3** (10)	90	81	*S*
6	(*S*)-**3** (5)	94	64	*S*
7	(*S*)-**4** (10)	92	31	*S*

[a] $Ti(O^iPr)_4/Et_2Zn$/benzaldehyde = 1.2:3:1; reaction temperature: r.t.; reaction time: 5 h.
[b] Isolated yield.
[c] Data were determined by GC analysis using a chiral column (Chiral beta-DEX 120 capillary column).
[d] The absolute configuration of the products were determined by comparison to the literature data.

Table 3
Addition of diethylzinc (1.5 M in hexane) to aldehydes using ligands (*S*)-**3** in the presence of titanium tetraisopropoxide



Entry	R[a]	Yield (%)[b]	ee (%)[c]	Config.[d]
1	Ph	93	89	*S*
2	*p*-ClC_6H_4	92	88	*S*
3	*p*-BrC_6H_4	92	90	*S*
4	*p*-$MeOC_6H_4$	85	74	*S*
5	*o*-$MeOC_6H_4$	87	90	*S*
6	PhCH = CH	94	80	*S*
7	1-Naphthyl	96	85	*S*

[a] (*S*)-**3**/$Ti(O^iPr)_4$/Et_2Zn/aldehyde = 0.2:1.2:3:1; reaction temperature: r.t.; reaction time: 5 h.
[b] Isolated yield.
[c] Data were determined by GC analysis using a chiral column (Chiral beta-DEX 120 capillary column).
[d] The absolute configuration of the products were determined by comparison to the literature data.

3. Conclusions

In conclusion, we have prepared aminonaphthol and imine type ligands (*S*)-**1**–**4** from (*S*)-3-formyl BINOL conveniently. Their catalytic effectivities were tested by the ethylation of Et_2Zn to aldehydes, and the imine type ligand (*S*)-**3** gave the best results with high yields and good ee values in the presence of $Ti(O^iPr)_4$.

4. Experimental

4.1. General

The ^1H and ^{13}C NMR spectra were recorded on a Bruker AC-300 instrument in $CDCl_3$ solution with TMS as internal standard. Optical rotations were measured on a Perkin–Elmer 241 polarimeter. IR spectra were recorded as KBr plates on a Bruker Equinox 55 spectrometer. The high-resolution mass spectra (MALDI-HRMS) were measured on an Ionspec FT MS 7.0 T spectrometer. All experiments which are sensitive to moisture or air were carried out under an argon atmosphere using standard Schlenk techniques. Diethylzinc (1.5 M solution in hexane) was purchased from Aldrich. All anhydrous solvents were purified and dried by standard techniques just before use.

4.2. Typical procedure for the preparation of (*S*)-*1* and (*S*)-*2*

Under an argon atmosphere (*S*)-**3**-formyl BINOL (2 mmol) and morpholine or piperidine (2.4 mmol) were mixed in THF (20 mL) and MeOH (5 mL) in the presence of 4 Å molecular sieves at room temperature. After refluxing for 4 h, the reaction mixture was cooled to 0 °C. Sodium borohydride (4 mmol) was added portionwise and the resulting mixture was continuously stirred at room temperature for 0.5 h. The reaction was then quenched with 1 M NaOH and the reaction mixture was extracted with EtOAc. The extract was washed with saturated NaCl solution and dried over Na_2SO_4. After removal of the solvent, the residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate (3/1) as eluent.

4.2.1. (*S*)-*3*-morpholinomethyl-1,1′-binaphthol [(*S*)-*1*]

White solid; yield: 96%; $[\alpha]_D^{25} = -32.5$ ($c = 0.1$, CH_2Cl_2); m.p. 216–218 °C; ^1H NMR (300 MHz, $CDCl_3$) δ: 2.65 (s, 4H), 3.70 (s, 4H), 3.97–4.05 (m, 2H), 5.06 (br, 1H), 7.10-7.38 (m, 7H), 7.73–7.92 (m, 4H).

4.2.2. (*S*)-*3*-piperidinomethyl-1,1′-binaphthol [(*S*)-*2*]

White solid; yield: 92%; $[\alpha]_D^{25} = -34.7$ ($c = 0.1$, CH_2Cl_2); m.p. 146–148 °C; ^1H NMR (300 MHz, $CDCl_3$) δ: 1.46 (br, 2H), 1.57–1.60 (m, 4H), 2.58 (br, 4H), 3.93–3.99 (m, 2H), 7.13–7.38 (m, 7H), 7.68–7.91 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 24.0, 25.7, 54.1, 62.7, 110.0, 112.6, 115.4, 117.8, 123.4, 123.7, 124.7, 125.2, 126.5, 127.0, 127.9, 128.4, 128.5, 129.1, 129.5, 130.0, 133.8, 134.1, 151.5, 155.6; IR (KBr): 3313, 2937, 1622, 1506, 1427, 812, 740 cm^{-1}; HR-MS Calc. for $C_{26}H_{26}NO_2$ (M^++H): 384.1964. Found: 384.1954.

4.3. Preparation of (*S*)-*3*-(*N*-hydroxyl)iminoformyl-1,1′-binaphthol [(*S*)-*3*]

To a solution of (*S*)-**3**-formyl BINOL (2 mmol) in dry EtOH (20 mL) were added NaOAc (4 mmol), powdered and activated 4 Å molecular sieves (excess) and hydroxylamine hydrochloride (2.4 mmol) in turn. The mixture was stirred under reflux for 12 h. The 4 Å MS were filtered off and the solvent was evaporated under vacuum. To the residue were added EtOAc (20 mL) and water (20 mL). After shaking the organic layer was separated, dried over Na_2SO_4 and concentrated to solvent free. The remaining solid was recrystallized from petroleum ether/dichloromethane to give a pale yellow solid. Yield: 85%; $[\alpha]_D^{25} = -89.6$ ($c = 0.1$, CH_2Cl_2); m.p. 254–256 °C; ^1H NMR (300 MHz, $CDCl_3$)δ: 4.98 (s, 1H), 7.08–7.41 (m, 7H), 7.86–7.95 (m, 3H), 8.50 (s, 1H), 9.97 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 110.1, 112.4, 114.3, 118.6, 122.8, 123.6, 124.8, 126.2, 126.4, 127.7, 128.2, 128.4, 128.7, 129.1, 129.4, 130.7, 131.8, 134.6, 138.1, 145.7, 151.9; IR (KBr): 3342, 1622, 1586, 1506, 1427, 1340, 1282, 812, 740 cm^{-1}; HR-MS Calc. for $C_{21}H_{16}NO_3$ (M^++H): 330.1130. Found: 330.1119.

4.4. Preparation of (*S*)-*3*-(*N*-pyridin-2-yl)iminoformyl-1,1′-binaphthol [(*S*)-*4*]

To a solution of (*S*)-**3**-formyl BINOL (2 mmol) in dry EtOH (20 mL) were added 4 Å MS (excess) and 2-aminopyridine (2.4 mmol). The mixture was stirred under reflux for 12 h. The 4 Å MS were filtered off, and the solvent was evaporated under vacuum. The remaining solid was

recrystallized from petroleum ether/dichloromethane to give a yellow solid. Yield: 70%; $[\alpha]_D^{25} = -207$ ($c = 0.1$, CH_2Cl_2); m.p. 258–260 °C; ^1H NMR (300 MHz, $CDCl_3$) δ: 5.12 (s, 1H), 7.15–7.41 (m, 8H), 7.74–7.97 (m, 4H), 8.31 (s, 1H), 8.54 (s, 1H), 9.77 (s, 1H), 13.57 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 110.0, 114.2, 114.5, 117.9, 121.3, 121.4, 123.4, 123.6, 124.4, 124.9, 125.0, 126.8, 127.7, 128.2, 128.5, 129.6, 130.0, 130.4, 133.8, 137.5, 138.9, 149.2, 151.8, 156.1, 158.8, 164.6; IR (KBr): 3053, 1588, 1551, 1522, 1464, 1420, 808, 735 cm^{-1}; HR-MS Calc. for $C_{26}H_{19}N_2O_2$ (M^++H): 391.1446. Found: 391.1432.

4.5. General procedure for the asymmetric addition of diethylzinc to aldehydes

Procedure A (Table 1): To a solution of (*S*)-**3** (0.05 mmol) in toluene (3 mL) was added diethylzinc (2.0 mL, 1.5 M solution in hexane). After stirring at room temperature for 0.5 h, benzaldehyde was added and the mixture was stirred for 48 h. The reaction was quenched with 20 mL of saturated NH_4Cl solution, and the mixture was extracted with ethyl acetate (3×20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated to solvent free. The residue was purified by column chromatography on silica gel.

Procedure B (Tables 2 and 3): Titanium tetraisopropoxide (1.2 mmol) was added to a solution of (*S*)-**3** (0.2 mmol) in 3 mL of toluene at room temperature and the mixture was stirred for 15 min followed by addition of diethylzinc (2.0 mL, 1.5 M solution in hexane). After 15 min, benzaldehyde was added and the mixture was stirred at room temperature for 5 h. The reaction was quenched with 20 mL of saturated NH_4Cl solution, and the mixture was extracted with ethyl acetate (3×20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated to solvent free. The residue was purified by column chromatography on silica gel.

Acknowledgement

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Appendix A. Supplementary material

CCDC 640939 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2007.07.003.

References

[1] (a) For reviews R. Noyori, M. Kitamura, Angew. Chem., Int. Ed. Engl. 30 (1991) 49;
(b) K. Soai, S. Niwa, Chem. Rev. 92 (1992) 833;
(c) L. Pu, H.-B. Yu, Chem. Rev. 101 (2001) 757.
[2] (a) K. Soai, S. Yokoyama, T. Hayasaka, J. Org. Chem. 56 (1991) 4264;
(b) M.R. Paleo, I. Cabeza, J. Sardina, J. Org. Chem. 65 (2000) 2108;
(c) S. Superchi, T. Mecca, E. Giorgio, C. Rosini, Tetrahedron: Asymmetry 12 (2001) 1235;
(d) J. Priego, O.G. Mancheno, S. Cabrera, J.C. Carretero, J. Org. Chem. 67 (2002) 1346;
(e) M. Fontes, X. Verdaguer, L. Sola, M. Pericas, A. Riera, J. Org. Chem. 69 (2004) 2532.
[3] (a) E. Rijnberg, J.T.B.H. Jastrzebski, M.D. Janssen, J. Boersma, G.V. Koten, Tetrahedron Lett. 35 (1994) 6521;
(b) J.C. Anderson, M. Harding, Chem. Commun. (1998) 393.
[4] (a) C. Cardellicchio, G. Ciccarella, F. Naso, F. Perna, P. Tortorella, Tetrahedron 55 (1999) 14685;
(b) D.-X. Liu, L.-C. Zhang, Q. Wang, C.-S. Da, Z.-Q. Xin, R. Wang, M.C.K. Choi, A.S.C. Chan, Org. Lett. 3 (2001) 2733.
[5] (a) T. Mino, K. Oishi, M. Yamashita, Synlett (1998) 965;
(b) R. Fleischer, M. Braun, Synlett (1998) 1441;
(c) D. Guijarro, P. Pinho, P.G. Andersson, J. Org. Chem. 63 (1998) 2530;
(d) B.D. Dangel, R. Polt, Org. Lett. 2 (2000) 3003;
(e) M. Braun, R. Fleischer, B. Mai, M.-A. Schneider, S. Lachenicht, Adv. Syn. Catal. 346 (2004) 474.
[6] (a) B. Schmidt, D. Seebach, Angew. Chem., Int. Ed. Engl. 30 (1991) 1321;
(b) D. Seebach, A.K. Beck, B. Schmidt, Y.M. Wang, Tetrahedron 50 (1994) 4363;
(c) B. Weber, D. Seebach, Tetrahedron 50 (1994) 7473;
(d) F.Y. Zhang, C.W. Yip, R. Cao, A.S.C. Chan, Tetrahedron: Asymmetry 8 (1997) 585;
(e) F.Y. Zhang, A.S.C. Chan, Tetrahedron: Asymmetry 8 (1997) 3651;
(f) P.B. Rheiner, H. Sellner, D. Seebach, Helv. Chem. Acta 80 (1997) 2027.
[7] (a) S. Vyskocil, S. Jaracz, M. Smrcina, M. Sticha, V. Hanus, M. Polasek, P. Kocovsky, J. Org. Chem. 63 (1998) 7727;
(b) G. Bringmann, M. Breuning, Tetrahedron: Asymmetry 9 (1998) 667;
(c) D.-H. Ko, K.- H. Kim, D.-C. Ha, Org. Lett. 4 (2002) 3759.
[8] (a) M. Shi, C.-J. Wang, Tetrahedron: Asymmetry 13 (2002) 2161;
(b) T. Mino, A. Suzuki, M. Yamashita, S. Narita, Y. Shirae, M. Sakamoto, T. Fujita, J. Organomet. Chem. 691 (2006) 4297.
[9] E.F. Dimauro, M.C. Kozlowski, Org. Lett. 3 (2001) 1641.
[10] Y.-C. Qin, L. Liu, L. Pu, Org. Lett. 7 (2005) 2381.
[11] A.F. Abdel-Magid, K.G. Carson, B.D. Harris, C.A. Maryanoff, R.D. Shah, J. Org. Chem. 61 (1996) 3849.
[12] (a) Y. Wang, T.D.P. Stack, J. Am. Chem. Soc. 118 (1996) 13097;
(b) X.G. Zhou, J.S. Huang, P.H. Ko, K.K. Cheung, C.M. Che, J. Chem. Soc., Dalton Trans. (1999) 3303.
[13] Crystal data for *rac*-3 · THF: $C_{25}H_{23}NO_4$, $M = 401.44$, triclinic, space group $P\bar{1}$, $a = 8.823(8)$ Å, $b = 11.487(8)$ Å, $c = 11.591(9)$ Å, $\alpha = 62.78(3)°$, $\beta = 78.67(4)°$, $\gamma = 76.47(4)°$, $V = 1010.2(14)$ Å^3, $Z = 2$, $D_c = 1.320$ g cm^{-3}, Mo Kα ($\lambda = 0.71070$ Å), $T = 113(2)$ K, $\mu = 0.089$ mm^{-1}, crystal size (mm) $0.16 \times 0.16 \times 0.16$. Area detector data were collected on a MicroMax-007 diffractometer. A total of 7655 reflections were collected ($1.99 < \theta < 25.02$). Structure solution by direct method (SHELXS-97), refinement by full-matrix least squares on F^2, $R_1 = 0.0840$, $wR_2 = 0.2527$, GOF = 1.199.