Pergamon

Tetrahedron: *Asymmetry* 9 (1998) 3911–3917

TETRAHEDRON: *ASYMMETRY*

Synthesis of new chiral catalysts, pyridyl- and bipyridylalcohols, for the enantioselective addition of diethylzinc to benzaldehyde

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Received 21 September 1998; accepted 29 September 1998

Abstract

New chiral ligands, pyridyl- and bipyridylalcohols, were prepared and their catalytic role in the reaction of diethylzinc with benzaldehyde to give 1-phenyl-1-propanol was studied. In several cases, the yields approach 100%, and ee-values of up to 86% are observed.

1. Introduction

Pyridine derivatives designed as ligands for metal complexes with predetermined helical chirality have recently been synthesized.[1,2] The development of this synthetic method opens up the possibility of preparing a series of ligands that are useful in enantioselective catalysis. Many pyridylalcohols have proved to be efficient catalysts in the asymmetric addition of dialkylzinc to aldehydes.[3] We report here the preparation of new chiral ligands and their use as catalysts in the addition reaction of diethylzinc to benzaldehyde.

2. Preparation of ligands

The bipyridine **1** and the pyridine **9** were synthesized according to literature procedures.[1,3i] The lithiation of **1** and **9** occurs stereoselectively and predefines the configuration of C8 (cf. Scheme 1). The solutions of lithiated **1** or **9** react with several ketones to give the alcohols **2–8** or **10–16**. When a prochiral ketone is used, a new stereogenic center is introduced in the side chain at C1″ (cf. Scheme 1). Depending on the ketone, either only one diastereomer (with 1-acetonaphthone), or a pair of diastereomers (with acetophenone and 2-acetonaphthone) is obtained (cf. Scheme 2). The diastereomers are efficiently

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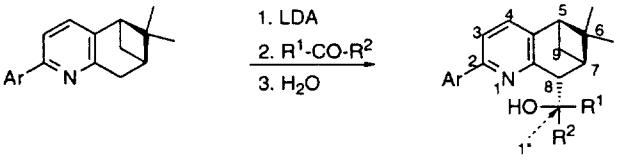
0957-4166/98/$ - see front matter
PII: S0957-4166(98)00399-1

separated by column chromatography. The structure of ligand **14** was determined by X-ray diffraction. Thus it was possible to establish the absolute configuration of the chiral center C1″, which is *S*. The ^{1}H NMR measurements were used to determine the correct absolute configuration of C1″ for the other ligands. For the ligands with *R*-configured C1″, **5**, **8**, **13** and **16**, the chemical shifts of H(9)endo (strongly shielded by the aromatic substituent) are −0.06 to −0.08 ppm. For the *S*-configured ligands, **4**, **6**, **7**, **12**, **14** and **15**, no shielding occurs and the chemical shifts of H(9)endo are 1.61 to 1.56 ppm.



Scheme 1.

These ligands can be classified into two categories: tridentate ligands (**2–8**, Ar=2-pyridyl) and bidentate ligands (**9–16**, Ar=phenyl). All ligands are derived from (−)-α-pinene, which results in each case in an *S*-configured C8-center. Since (+)-α-pinene is also available, all ligands can also be prepared in the other enantiomeric form.

3. Catalyzed addition of diethylzinc to benzaldehyde

Having prepared these ligands, we studied their properties as catalysts for the enantioselective addition of diethylzinc to benzaldehyde (Scheme 3 and Table 1). The standardized procedure for the catalytic reaction is given in the experimental section.

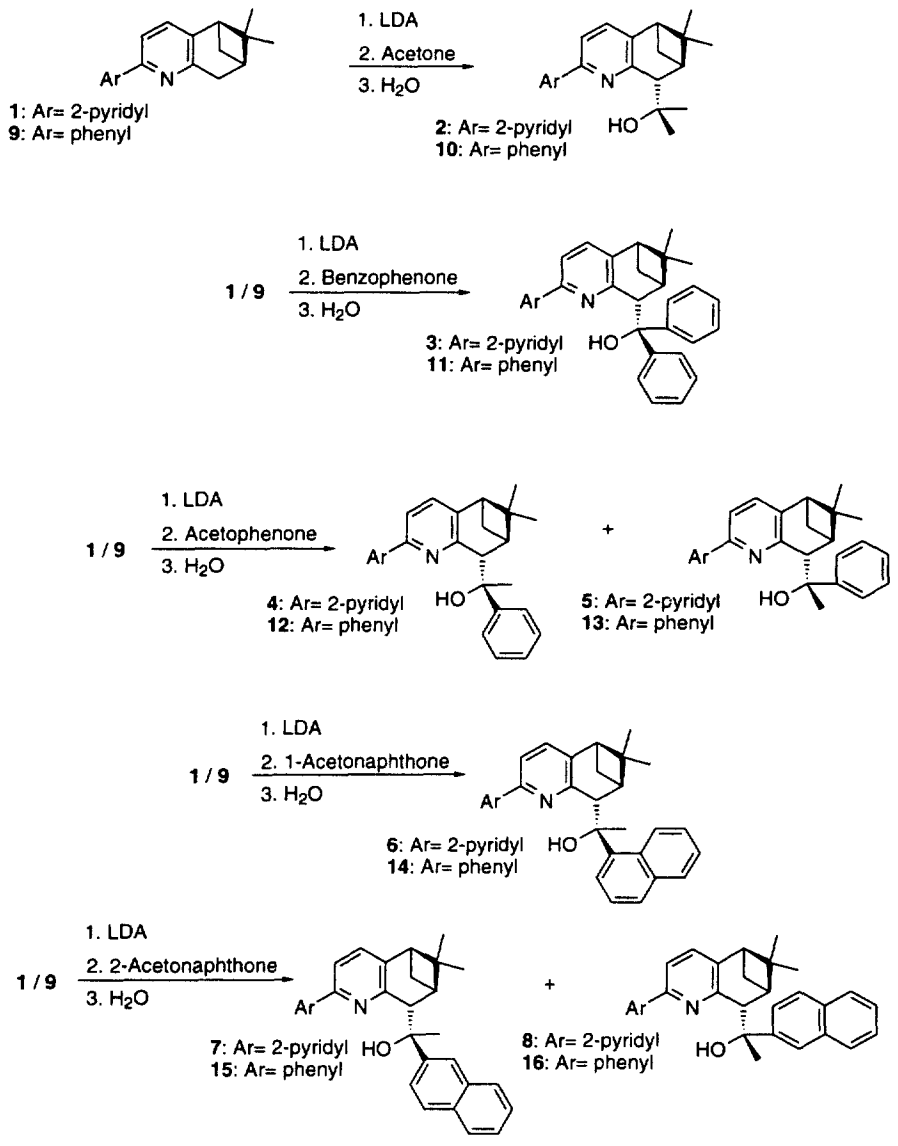
All ligands mainly induce the formation of the *R*-enantiomer of 1-phenyl-1-propanol with the noticeable exception of ligand **10** inducing the formation of the *S*-enantiomer.

By comparison of corresponding tri- and bidentate ligands (**2/10**, **3/11**, **4/12**, **5/13**, **6/14**, **7/15**, **8/16**), higher ee-values and also generally higher yields are found for the tridentate bipyridine derivatives. Although no quantitative investigations were carried out, this behavior is most likely due to a higher thermodynamic stability of the zinc/catalyst precursor complex that is involved in the transition state of the addition reaction.

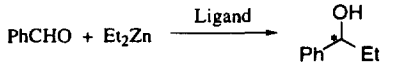
Chirality at the C1″ center is not a prerequisite for a high enantioselectivity. Ligands **3** and **11**, where C1″ is not a stereogenic center, induce higher ees, when compared to some other ligands, where C1″ is a stereogenic center. The most important contribution to the enantioselective induction seems to be due to the configuration at C8.

This is corroborated by the observation that the four epimeric pairs of ligands **4/5**, **7/8**, **12/13** and **15/16**, which differ only in their absolute configuration at C1″, all give the same enantiomer of the product of the catalytic reaction, however with very different efficiencies. The epimers of the pair with an *S*-configuration at C1″, **4**, **7**, **12** and **15**, are systematically better catalysts than those with *R*-configuration at C1″, **5**, **8**, **13** and **16**. The stereoselectivity is mainly influenced by the configuration at C1″. In the ligands with *S*-configuration at C1″, the aryl substituent is in an equatorial position, making the complex stereochemically more selective.

Ligand **10**, with methyl groups at C1″, is the only case where the product of the catalytic reaction is formed in the opposite (*S*) configuration, with 42% ee. The corresponding tridentate ligand **2** yields the alcohol in the *R*-configuration with 73% ee. This behavior is not easy to understand, but it hints at a different mechanism for the reaction for ligand **10**.



Scheme 2.



Scheme 3.

4. Experimental

4.1. General

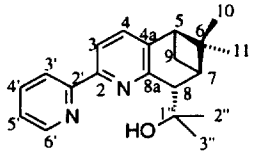
All experiments were carried out under an inert atmosphere using dry, distilled solvents. ^{1}H NMR spectra were recorded on a Varian Gemini 300 MHz or a Bruker DRX 500 MHz in $CDCl_3$, and chemical shifts are referenced relative to $CDCl_3$ (δ=7.24 ppm). Mass spectra were recorded on a Bruker Apex II FT/ICR spectrometer. Optical rotations were performed using a Perkin–Elmer 241 MC polarimeter,

Table 1
Enantioselective addition of diethylzinc to benzaldehyde[a]

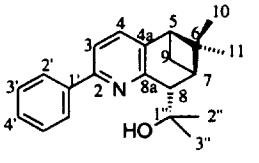
Ligand	Reac. time (h)	Yield (%)[b]	ee (%)[b]	Config.[c]
2	1	100	73	*R*
3	1	100	79	*R*
4	1	100	78	*R*
5	1	100	52	*R*
6	1	99	86	*R*
7	1	100	82	*R*
8	1	99	47	*R*
10	8	91	42	*S*
11	6	90	68	*R*
12	8	91	45	*R*
13	8	60	18	*R*
14	24	91	64	*R*
15	24	95	46	*R*
16	24	85	15	*R*

a) All reactions were carried out at 0°C in toluene-hexane (1:1); b) Determined by GC analysis using a β-DEX™110 capillary column from SUPELCO; c) Determined by comparison with the chromatograms of enantiomerically pure samples of *R*- and *S*-1-phenyl-1-propanol.

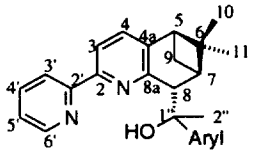
and concentration (c) is given in g/100 ml). The enantiomeric excess of the diethylzinc adducts was determined by GC analysis using a β-DEX™110 capillary column from SUPELCO. The ligands **2–8** and **9–16** are numbered as follows.



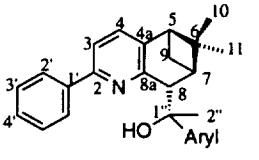
2



10



3 - 8



11 - 16

4.2. *General procedure for the synthesis of ligands 2–8 and 10–16*

A 100 ml Schlenk flask was filled with 30 ml dry THF and cooled to −40°C. Diisopropylamine (1.2 ml, 8 mmol) and n-butyllithium (1.6 M solution in hexane, 4.8 ml, 7.7 mmol) were added with stirring. The temperature was raised to 0°C for 30 min. The mixture was cooled to −60°C and **1** (or **9**) (4 mmol), dissolved in 4 ml dry THF, was slowly added. The dark mixture was kept at −50°C for 2 h. A solution of 4 mmol of the desired ketone in 10 ml dry THF was added over 4 h and after an additional hour, the

reaction was quenched with 15 ml of water. The THF was evaporated and the aqueous phase extracted twice with 25 ml of dichloromethane. The solvent was evaporated and the crude product dried under vacuum.

Ligand **2** was obtained in good purity from the crude reaction mixture (90% yield); $[\alpha]_D^{25}$=+29.2 (c 0.620, $CHCl_3$); ^{1}H NMR: 8.64 (ddd, 1H, H(6′), $^3J_{6',5'}$ 4.8 Hz, $^4J_{6',4'}$ 1.8 Hz, $^5J_{6',3'}$ 0.9 Hz), 8.16 (ddd, 1H, H(3′), $^3J_{3',4'}$ 7.9 Hz, $^4J_{3',5'}$ 1.1 Hz, $^5J_{3',6'}$ 0.9 Hz), 8.16 (d, 1H, H(3), $^3J_{3,4}$ 7.9 Hz), 8.12 (s, 1H, OH), 7.75 (ddd, 1H, H(4′), $^3J_{4',3'}$ 7.9 Hz, $^3J_{4',5'}$ 7.6 Hz, $^4J_{4',6'}$ 1.8 Hz), 7.40 (d, 1H, H(4), $^3J_{4,3}$ 7.9 Hz), 7.26 (ddd, 1H, H(5′), $^3J_{5',4'}$ 7.6 Hz, $^3J_{5',6'}$ 4.8 Hz, $^4J_{5',3'}$ 1.1 Hz), 3.27 (d, 1H, H(8), $^3J_{8,7}$ 1.9 Hz), 2.80 (dd, 1H, H(5), $^3J_{5,9exo}$ 5.8 Hz, $^4J_{5,7}$ 5.8 Hz), 2.61 (ddd, 1H, H(9exo), $^2J_{9exo,9endo}$ 9.9 Hz, $^3J_{9exo,5}$ 5.8 Hz, $^3J_{9exo,7}$ 5.8 Hz), 2.36 (ddd, 1H, H(7), $^3J_{7,9exo}$ 5.8 Hz, $^4J_{7,5}$ 5.8 Hz, $^3J_{7,8}$ 1.9 Hz), 1.44 (s, 3H, H(11)), 1.43 (d, 1H, H(9endo), $^2J_{9endo,9exo}$ 9.9 Hz), 1.34 (s, 3H, H(2″)), 1.11 (s, 3H, H(3″)), 0.70 (s, 3H, H(10)); ESI-MS: 309.1965.

Ligands **3–5** have been prepared previously.[4]

Ligand **6** was recrystallized from hexane:diethyl ether (50% yield); $[\alpha]_D^{25}$=+285.0 (c 0.061, $CHCl_3$); ^{1}H NMR: 9.52 (d, 1H, J 8.3 Hz), 8.71 (ddd, 1H, H(6′), $^3J_{6',5'}$ 4.9 Hz, $^4J_{6',4'}$ 1.8 Hz, $^5J_{6',3'}$ 1.0 Hz), 8.51 (s, 1H, OH), 8.35 (ddd, 1H, H(3′), $^3J_{3',4'}$ 8.1 Hz, $^4J_{3',5'}$ 1.1 Hz, $^5J_{3',6'}$ 1.0 Hz), 8.25 (d, 1H, H(3), $^3J_{3,4}$ 7.9 Hz), 7.83 (ddd, 1H, H(4′), $^3J_{4',3'}$ 8.1 Hz, $^3J_{4',5'}$ 7.5 Hz, $^4J_{4',6'}$ 1.8 Hz), 7.87–7.78 (m, 2H), 7.46 (d, 1H, H(4), $^3J_{4,3}$ 7.9 Hz), 7.52–7.37 (m, 4H), 7.31 (ddd, 1H, H(5′), $^3J_{5',4'}$ 7.5 Hz, $^3J_{5',6'}$ 4.9 Hz, $^4J_{5',3'}$ 1.1 Hz), 4.41 (d, 1H, H(8), $^3J_{8,7}$ 1.7 Hz), 2.76 (dd, 1H, H(5), $^3J_{5,9exo}$ 5.7 Hz, $^4J_{5,7}$ 5.7 Hz), 2.55 (ddd, 1H, H(9exo), $^2J_{9exo,9endo}$ 9.9 Hz, $^3J_{9exo,5}$ 5.7 Hz, $^3J_{9exo,7}$ 5.7 Hz), 1.75 (s, 3H, H(2″)), 1.56 (d, 1H, H(9endo), $^2J_{9endo,9exo}$ 9.9 Hz), 1.48 (ddd, 1H, H(7), $^3J_{7,9exo}$ 5.7 Hz, $^4J_{7,5}$ 5.7 Hz, $^3J_{7,8}$ 1.7 Hz), 1.12 (s, 3H, H(11)), 0.50 (s, 3H, H(10)); ESI-MS: 421.2276.

Ligand **7** was separated by column chromatography (hexane:diethyl ether:triethylamine 5:1:0.1) then recrystallized from hexane:diethyl ether (45% yield); $[\alpha]_D^{25}$=−210.9 (0.060, $CHCl_3$); ^{1}H NMR: 8.68 (ddd, 1H, H(6′), $^3J_{6',5'}$ 4.8 Hz, $^4J_{6',4'}$ 1.8 Hz, $^5J_{6',3'}$ 0.9 Hz), 8.66 (s, 1H, OH), 8.29 (ddd, 1H, H(3′), $^3J_{3',4'}$ 8.0 Hz, $^4J_{3',5'}$ 1.0 Hz, $^5J_{3',6'}$ 1.0 Hz), 8.23 (d, 1H, H(3), $^3J_{3,4}$ 7.9 Hz), 8.04 (m, 1H), 7.91–7.81 (m, 4H), 7.82 (ddd, 1H, H(4′), $^3J_{4',3'}$ 8.0 Hz, $^3J_{4',5'}$ 7.5 Hz, $^4J_{4',6'}$ 1.8 Hz), 7.49–7.46 (m, 2H), 7.46 (d, 1H, H(4), $^3J_{4,3}$ 7.9 Hz), 7.30 (ddd, 1H, H(5′), $^3J_{5',4'}$ 7.5 Hz, $^3J_{5',6'}$ 4.8 Hz, $^4J_{5',3'}$ 1.1 Hz), 3.56 (d, 1H, H(8), $^3J_{8,7}$ 1.8 Hz), 2.79 (dd, 1H, H(5), $^3J_{5,9exo}$ 5.8 Hz, $^4J_{5,7}$ 5.8 Hz), 2.60 (ddd, 1H, H(9exo), $^2J_{9exo,9endo}$ 9.9 Hz, $^3J_{9exo,5}$ 5.8 Hz, $^3J_{9exo,7}$ 5.8 Hz), 1.82 (ddd, 1H, H(7), $^3J_{7,9exo}$ 5.8 Hz, $^4J_{7,5}$ 5.8 Hz, $^3J_{7,8}$ 1.8 Hz), 1.66 (s, 3H, H(2″)), 1.61 (d, 1H, H(9endo), $^2J_{9endo,9exo}$ 9.9 Hz), 1.21 (s, 3H, H(11)), 0.58 (s, 3H, H(10)); ESI-MS: 421.2275.

Ligand **8** was separated by column chromatography (hexane:diethyl ether:triethylamine 5:1:0.1) then recrystallized from hexane:diethyl ether (15% yield); $[\alpha]_D^{25}$=+457.3 (c 0.061, $CHCl_3$); ^{1}H NMR: 9.67 (s, 1H, OH), 8.71 (ddd, 1H, H(6′), $^3J_{6',5'}$ 4.8 Hz, $^4J_{6',4'}$ 1.8 Hz, $^5J_{6',3'}$ 0.9 Hz), 8.42 (ddd, 1H, H(3′), $^3J_{3',4'}$ 7.9 Hz, $^4J_{3',5'}$ 0.9 Hz, $^5J_{3',6'}$ 0.9 Hz), 8.15 (d, 1H, H(3), $^3J_{3,4}$ 7.9 Hz), 7.88 (ddd, 1H, H(4′), $^3J_{4',3'}$ 7.9 Hz, $^3J_{4',5'}$ 7.9 Hz, $^4J_{4',6'}$ 1.8 Hz), 7.68–7.59 (m, 3H), 7.54 (d, 1H, J 8.8 Hz), 7.37–7.31 (m, 3H), 7.31 (ddd, 1H, H(5′), $^3J_{5',4'}$ 7.9 Hz, $^3J_{5',6'}$ 4.8 Hz, $^4J_{5',3'}$ 0.9 Hz), 7.22 (d, 1H, H(4), $^3J_{4,3}$ 7.9 Hz), 3.60 (d, 1H, H(8), $^3J_{8,7}$ 1.4 Hz), 2.56 (ddd, 1H, H(7), $^3J_{7,9exo}$ 5.6 Hz, $^4J_{7,5}$ 5.6 Hz, $^3J_{7,8}$ 1.4 Hz), 2.47 (dd, 1H, H(5), $^3J_{5,9exo}$ 5.6 Hz, $^4J_{5,6}$ 5.8 Hz), 2.05 (ddd, 1H, H(9exo), $^2J_{9exo,9endo}$ 10.3 Hz, $^3J_{9exo,5}$ 5.6 Hz, $^3J_{9exo,7}$ 5.6 Hz), 1.93 (s, 3H, H(2″)), 1.37 (s, 3H, H(11)), 0.69 (s, 3H, H(10)), −0.06 (d, 1H, H(9endo), $^2J_{9endo,9exo}$ 10.3 Hz); ESI-MS: 421.2271.

Ligand **10** was purified by column chromatography (hexane:ethyl acetate 7:1; 45% yield); $[\alpha]_D^{25}$=+39.8 (c 0.294, $CHCl_3$); ^{1}H NMR: 8.13 (s, 1H, OH), 7.89 (dd, 2H, H(2′), $^3J_{2',3'}$ 8.3 Hz, $^4J_{2',4'}$ 1.4 Hz), 7.50–7.31 (m, 5H), 3.27 (d, 1H, H(8), $^3J_{8,7}$ 1.8 Hz), 2.77 (dd, 1H, H(5), $^3J_{5,9exo}$ 5.7 Hz, $^4J_{5,7}$ 5.7 Hz), 2.60 (ddd, 1H, H(9exo), $^2J_{9exo,9endo}$ 9.9 Hz, $^3J_{9exo,5}$ 5.7 Hz, $^3J_{9exo,7}$ 5.7 Hz), 2.35 (ddd, 1H,

H(7), $^3J_{7,9exo}$ 5.7 Hz, $^4J_{7,5}$ 5.7 Hz, $^3J_{7,8}$ 1.8 Hz), 1.43 (s, 3H, H(11)), 1.42 (d, 1H, H(9endo), $^2J_{9endo,9exo}$ 9.9 Hz), 1.33 (s, 3H, H(2″)), 1.10 (s, 3H, H(3″)), 0.71 (s, 3H, H(10)); ESI-MS: 308.2016.

Ligand **11** was purified by column chromatography (hexane:ethyl acetate 7:1; 50% yield); $[\alpha]_D^{25}$=+533.3 (c 0.061, $CHCl_3$); ^{1}H NMR: 10.2 (s, 1H, OH), 8.03 (dd, 2H, H(2′), $^3J_{2',3'}$ 8.2 Hz, $^4J_{2',4'}$ 1.4 Hz), 7.55–7.08 (m, 15H), 4.56 (d, 1H, H(8), $^3J_{8,7}$ 1.3 Hz), 2.62 (ddd, 1H, H(7), $^3J_{7,9exo}$ 5.7 Hz, $^4J_{7,5}$ 5.7 Hz, $^3J_{7,8}$ 1.3 Hz), 2.55 (dd, 1H, H(5), $^3J_{5,9exo}$ 5.7 Hz, $^4J_{5,7}$ 5.7 Hz), 2.06 (ddd, 1H, H(9exo), $^2J_{9exo,9endo}$ 10.3 Hz, $^3J_{9exo,5}$ 5.7 Hz, $^3J_{9exo,7}$ 5.7 Hz), 1.39 (s, 3H, H(11)), 0.89 (s, 3H, H(10)), −0.18 (d, 1H, H(9endo), $^2J_{9endo,9exo}$ 10.3 Hz); ESI-MS: 432.2334.

Ligand **12** was separated by column chromatography (hexane:diethyl ether:triethylamine 5:1:0.1; 25% yield); $[\alpha]_D^{25}$=−117.5 (c 0.061, $CHCl_3$); ^{1}H NMR: 8.64 (s, 1H, OH), 7.96 (dd, 2H, H(2′), $^3J_{2',3'}$ 8.3 Hz, $^4J_{2',4'}$ 1.4 Hz), 7.63–7.26 (m, 10H), 3.43 (d, 1H, H(8), $^3J_{8,7}$ 1.8 Hz), 2.75 (dd, 1H, H(5), $^3J_{5,9exo}$ 5.7 Hz, $^4J_{5,7}$ 5.7 Hz), 2.57 (ddd, 1H, H(9exo), $^2J_{9exo,9endo}$ 9.9 Hz, $^3J_{9exo,5}$ 5.7 Hz, $^3J_{9exo,7}$ 5.7 Hz), 1.79 (ddd, 1H, H(7), $^3J_{7,9exo}$ 5.7 Hz, $^4J_{7,5}$ 5.7 Hz, $^3J_{7,8}$ 1.8 Hz), 1.56 (d, 1H, H(9endo), $^2J_{9endo,9exo}$ 9.9 Hz), 1.53 (s, 3H, H(2″)), 1.25 (s, 3H, H(11)), 0.59 (s, 3H, H(10)); ESI-MS: 370.2195.

Ligand **13** was separated by column chromatography (hexane:diethyl ether:triethylamine 5:1:0.1; 15% yield); $[\alpha]_D^{25}$=−96.3 (c 0.316, $CHCl_3$); ^{1}H NMR: 9.71 (s, 1H, OH), 8.02 (dd, 2H, H(2′), $^3J_{2',3'}$ 8.4 Hz, $^4J_{2',4'}$ 1.4 Hz), 7.52–7.41 (m, 4H), 7.19–7.16 (m, 3H), 7.08–7.06 (m, 3H), 3.50 (d, 1H, H(8), $^3J_{8,7}$ 1.7 Hz), 2.49 (dd, 1H, H(5), $^3J_{5,9exo}$ 5.6 Hz, $^4J_{5,7}$ 5.6 Hz), 2.47 (ddd, 1H, H(7), $^3J_{7,9exo}$ 5.6 Hz, $^4J_{7,5}$ 5.6 Hz, $^3J_{7,8}$ 1.8 Hz), 2.09 (ddd, 1H, H(9exo), $^2J_{9exo,9endo}$ 10.3 Hz, $^3J_{9exo,5}$ 5.6 Hz, $^3J_{9exo,7}$ 5.6 Hz), 1.81 (s, 3H, H(2″)), 1.37 (s, 3H, H(11)), 0.67 (s, 3H, H(10)), −0.08 (d, 1H, H(9endo), $^2J_{9endo,9exo}$ 10.3 Hz); ESI-MS: 370.2194.

Ligand **14** was recrystallized from hexane:diethyl ether (30% yield); $[\alpha]_D^{25}$=−165.5 (c 0.060, $CHCl_3$); ^{1}H NMR: 9.50 (d, 1H, J 7.9 Hz), 8.65 (s, 1H, OH), 8.04–8.00 (m, 2H), 7.87–7.78 (m, 2H), 7.57–7.37 (m, 9H), 4.40 (d, 1H, H(8), $^3J_{8,7}$ 1.7 Hz), 2.73 (dd, 1H, H(5), $^3J_{5,9exo}$ 5.7 Hz, $^4J_{5,7}$ 5.7 Hz), 2.54 (ddd, 1H, H(9exo), $^2J_{9exo,9endo}$ 9.9 Hz, $^3J_{9exo,5}$ 5.7 Hz, $^3J_{9exo,7}$ 5.7 Hz), 1.76 (s, 3H, H(2″)), 1.56 (d, 1H, H(9endo), $^2J_{9endo,9exo}$ 9.9 Hz), 1.47 (ddd, 1H, H(7), $^3J_{7,9exo}$ 5.7 Hz, $^4J_{7,5}$ 5.7 Hz, $^3J_{7,8}$ 1.7 Hz), 1.12 (s, 3H, H(11)), 0.50 (s, 3H, H(10)); ESI-MS: 420.2325.

Ligand **15** was separated by column chromatography (hexane:diethyl ether:triethylamine 5:1:0.1) and recrystallized from hexane:diethyl ether (20% yield); $[\alpha]_D^{25}$=−146.6 (c 0.062, $CHCl_3$); ^{1}H NMR: 9.00 (s, 1H, OH), 8.04–7.98 (m, 3H), 7.90–7.80 (m, 4H), 7.58–7.39 (m, 7H), 3.60 (d, 1H, H(8), $^3J_{8,7}$ 1.8 Hz), 2.77 (dxd, 1H, H(5), $^3J_{5,9exo}$ 5.7 Hz, $^4J_{5,7}$ 5.7 Hz), 2.60 (ddd, 1H, H(9exo), $^2J_{9exo,9endo}$ 9.8 Hz, $^3J_{9exo,5}$ 5.7 Hz, $^3J_{9exo,7}$ 5.7 Hz), 1.80 (ddd, 1H, H(7), $^3J_{7,9exo}$ 5.7 Hz, $^4J_{7,5}$ 5.7 Hz, $^3J_{7,8}$ 1.8 Hz), 1.66 (s, 3H, H(2″)), 1.60 (d, 1H, H(9endo), $^2J_{9endo,9exo}$ 9.8 Hz), 1.20 (s, 3H, H(11)), 0.59 (s, 3H, H(10)); ESI-MS: 420.2358.

Ligand **16** was separated by column chromatography (hexane:diethyl ether:triethylamine 5:1:0.1) and recrystallized from hexane:diethyl ether (10% yield); $[\alpha]_D^{25}$=+605.3 (c 0.060, $CHCl_3$); ^{1}H NMR: 9.93 (s, 1H, OH), 8.07 (dd, 2H, H(2′), $^3J_{2',3'}$ 8.3 Hz, $^4J_{2',4'}$ 1.3 Hz), 7.70–7.46 (m, 8H), 7.35–7.28 (m, 3H), 7.16 (d, 1H, H(4), $^3J_{4,3}$ 8.0 Hz), 3.64 (d, 1H, H(8), $^3J_{8,7}$ 1.5 Hz), 2.57 (ddd, 1H, H(7), $^3J_{7,9exo}$ 5.8 Hz, $^4J_{7,5}$ 5.8 Hz, $^3J_{7,8}$ 1.5 Hz), 2.45 (dd, 1H, H(5), $^3J_{5,9exo}$ 5.8 Hz, $^4J_{5,7}$ 5.8 Hz), 2.07 (ddd, 1H, H(9exo), $^2J_{9exo,9endo}$ 10.2 Hz, $^3J_{9exo,5}$ 5.8 Hz, $^3J_{9exo,7}$ 5.8 Hz), 1.93 (s, 3H, H(2″)), 1.38 (s, 3H, H(11)), 0.70 (s, 3H, H(10)), −0.06 (d, 1H, H(9endo), $^2J_{9endo,9exo}$ 10.2 Hz); ESI-MS: 420.2335.

4.3. Representative procedure for the catalytic reaction

A dried 10 ml Schlenk flask was charged with 0.025 mmol of ligand, 1 ml of dry toluene, and 0.5 mmol (52 mg) of benzaldehyde and then cooled to 0°C. To this stirred solution, 1 ml of a 1 M solution of diethylzinc in hexane (1 mmol) was added dropwise over a 10 min period. After the required reaction

time, 5 ml of 1 M HCl was added. The reaction mixture was extracted with dichloromethane and the organic layer was dried over Na_2SO_4. After removal of the solvent, the remaining oil was analyzed by GC to determine the conversion ratio of the benzaldehyde and the ee of the 1-phenyl-1-propanol.

Acknowledgements

This work was supported by the Swiss National Science Foundation. The authors thank Prof. Dr. P. Belser for the optical rotation measurements and Fredy Nydegger for the ESI-MS measurements.

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