Enantioselective Addition of Diethylzinc to Aldehydes Catalyzed by (1*R*,2*R*)-10-(Dialkylamino)isoborneols

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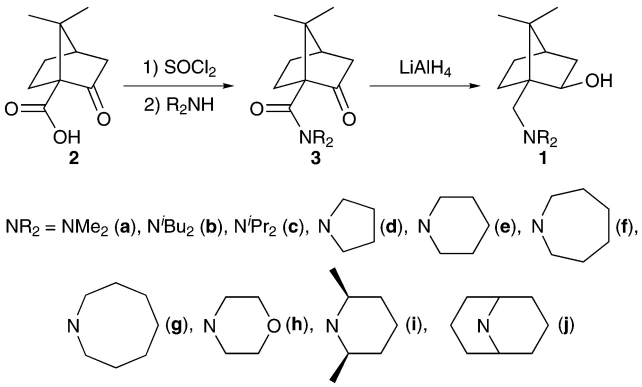
Abstract: (1*R*,2*R*)-10-Dialkylaminoisoborneols, γ-amino alcohol-type ligands, were synthesized from (+)-ketopinic acid. Their catalytic ability as a chiral ligand for enantioselective addition of diethylzinc to aldehydes was evaluated. Among them, the ligand with a 9-azabicyclo[3.3.1]nonan-9-yl group as an amino moiety was the most effective and showed good enantioselectivity towards various aldehydes.

Key words: aldehydes, amino alcohols, diethylzinc, enantioselective addition, enantioselectivity

Since the report on enantioselective addition of diethylzinc to benzaldehyde catalyzed by β-amino alcohols derived from amino acids by Oguni and Omi,[1] chiral amino alcohols have attracted much attention as catalysts in this area and a large number of diverse ligand structures have been developed to date.[2] Among them, amino alcohols with an isoborneol structure as a chiral source are very promising. For example, 3-*exo*-(dimethylamino)isoborneol (DAIB)[3] and its morpholino analogue 3-*exo*-morpholinoisoborneol (MIB),[4] isoborneol-based β-amino alcohols, are well-known as excellent catalysts. In addition, interesting reports on isoborneol-based δ-amino alcohols, which would form a flexible seven-membered Zn-chelate compared to a rigid five-membered one with β-amino alcohols, have recently been published.[5] However, to our knowledge, only one example has been reported on the enantioselective addition of diethylzinc to benzaldehyde using 10-(diisopropylamino)isoborneol (**1c**), an isoborneol-based γ-amino alcohol, which would form a six-membered Zn-chelate, but this ligand only showed moderate asymmetric induction.[6] Under such background, we focused on 10-(dialkylamino)isoborneols **1** to develop new versatile γ-amino alcohol-type ligands.[7] In this paper, we describe the synthesis of 10-(dialkylamino)isoborneols **1a**,**b**,**d**–**j**, and evaluation of their asymmetric-inducing ability on the addition reaction of diethylzinc to aldehydes.

γ-Amino alcohols **1** were synthesized from (+)-ketopinic acid (**2**), easily prepared from camphorsulfonyl chloride,[8] in three steps (Scheme 1). Treatment of **2** with thionyl chloride,[9] followed by amidation of the resulting acyl chloride with various secondary amines led to the keto amides **3**. Reduction of **3** using $LiAlH_4$ successfully afforded the desired **1**.[10,11]



Scheme 1

First, amino alcohols **1a**–**h** were tested as a catalyst for the addition reaction of diethylzinc to benzaldehyde (Scheme 2 and Table 1). When benzaldehyde (1 mmol) was reacted with diethylzinc (2 mmol) in the presence of ligand **1a** (5 mol%), the dimethylamino derivative, in hexane at room temperature for 3 h, 1-phenylpropan-1-ol was obtained in 99% yield with 65% ee (entry 1). Replacement of **1a** by **1c**[6], the bulky diisopropylamino derivative, increased the enantiomeric excess to 73%, though the reaction was very slow (entry 3). The reaction using ligands **1d**–**h** bearing cyclic amino groups also smoothly proceeded to give the alcohol in high chemical yield (entries 4–8). Interestingly, in these cases, the ring size of an amino group had significant effect on the enantioselectivity and the piperidino derivative **1e** gave the best result in 77% ee (entry 5). From these results, the reaction seemed to be very sensitive to the steric hindrance and/or the ring size of an amino group;[12] therefore, we designed the ligands **1i** and **1j** bearing *cis*-2,6-dimethylpiperidino and 9-azabicyclo[3.3.1]nonan-9-yl groups as an amino moiety. As expected, the use of ligand **1i** led to an increase in enantioselectivity (87% ee) with 95% chemical yield (entry 9). Interestingly, when benzaldehyde was added to a mixture of diethylzinc and ligand **1i** at 0 °C and then the reaction was carried out at room temperature, both the enantioselectivity and chemical yield were slightly improved (entry 10). Under the conditions, ligand **1j** showed the best result with 99% yield and 94% ee (entry 11). Additionally, the reaction at 0 °C required prolonged reaction time and resulted in decrease of the chemical yield

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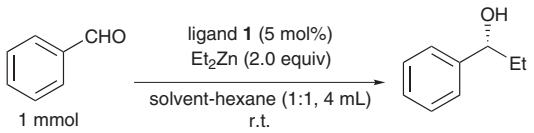
(entry 12). Hexane as a solvent was superior to toluene and Et_2O (entries 11, 13 and 14). All ligands used gave the alcohol with *R*-configuration, which would be formed via the transition state similar to the proposed one[13] with β-amino alcohols as shown in Figure 1.



Scheme 2

Table 1 Enantioselective Addition of Diethylzinc to Benzaldehyde Using Ligands **1a–j**

Entry	Ligand	Solvent	Time (h)	Yield (%)[a]	Ee (%)[b,c]
1	**1a**	hexane	3	99	65
2	**1b**	hexane	24	82	63
3	**1c**	hexane	24	83	73
4	**1d**	hexane	3	95	52
5	**1e**	hexane	3	96	77
6	**1f**	hexane	3	93	75
7	**1g**	hexane	3	93	56
8	**1h**	hexane	3	94	74
9	**1i**	hexane	3	95	87
10[d]	**1i**	hexane	3	99	90
11[d]	**1j**	hexane	3	99	94
12[e]	**1j**	hexane	6	91	94
13[d]	**1j**	toluene	3	90	93
14[d]	**1j**	Et_2O	3	95	92

[a] Isolated yield.
[b] Ee% was determined by HPLC.
[c] All configurations were determined to be *R* by optical rotation.
[d] Benzaldehyde was added at 0 °C.
[e] The reaction was carried out at 0 °C.

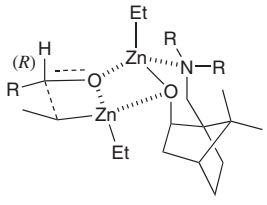


Figure 1 Transition state for asymmetric expression.

Next, using the most effective ligand **1j**, we examined the scope of the reaction (Table 2). The reaction with *p*-tolualdehyde, *p*-chlorobenzaldehyde, bulky *o*-tolualdehyde and 1-naphthaldehyde as aryl aldehydes smoothly proceeded and afforded the corresponding alcohols with high

Table 2 Enantioselective Addition of Diethylzinc to Aldehydes Using the Ligand **1j**[a]

Entry	Aldehyde	Time (h)	Yield (%)[b]	ee (%)[c,d]
1	*p*-tolualdehyde	3	99	93
2	*p*-chlorobenzaldehyde	3	99	92
3	*o*-tolualdehyde	3	99	95
4	1-naphthaldehyde	3	94	91
5	(*E*)-PhCH=CHCHO	3	86	79
6	$PhCH_2CH_2CHO$	3	82	84

[a] All reactions were carried out under the same conditions as entry 11 in Table 1.
[b] Isolated yield.
[c] Values were determined by HPLC.
[d] All configurations were determined to be *R* by optical rotation.

enantioselectivity (entries 1–4). Other aldehydes such as (*E*)-cinnamaldehyde or 3-phenylpropionaldehyde also gave the corresponding alcohols with enantiomeric excess up to 84% (entries 5 and 6).

In conclusion, we have designed isoborneol-based γ-amino alcohol ligands and evaluated their ability as a chiral catalyst on the addition reaction of diethylzinc to aldehydes. Among them, the ligand containing a 9-azabicyclo[3.3.1]nonan-9-yl group as an amino moiety was found to be the most effective and gave good enantioselectivity for various aldehydes. Further studies on application of this new catalyst to other asymmetric reactions are now under way.

IR spectra were recorded on a Shimadzu FTIR-8400S spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Jeol JNM-EX-270 spectrometer (^1H, 270 MHz; ^{13}C, 67.8 MHz). Mass spectra were recorded on a Jeol JMS-SX-102A spectrometer. Optical rotations were recorded on a Jasco DIP-370 instrument. For flash column chromatography, Fuji Silysia PQS-60B was used. Daicel Chemical Ind., Ltd. CHIRALCEL OD-H, CHIRALCEL OB-H or CHIRALPAK AD was used as the chiral column.

β-Keto Amides 3; (1*S*)-Dimethylketopinamide (3a); Typical Procedure

A solution of the acyl chloride, prepared from (+)-ketopinic acid (**2**; 1.00 g, 5.49 mmol) according to the reported method,[7] in THF (10 mL) was added to 50% aq Me_2NH (10 mL) at 0 °C. The mixture was stirred for 1 h at r.t. and was diluted with $CHCl_3$. The organic phase was washed by H_2O, aq 1 N HCl, H_2O and brine, and dried (Na_2SO_4). After filtration, the filtrate was removed in vacuo and the residue was purified by flash column chromatography (hexane–EtOAc, 3:1) to give **3a** (1.10 g, 96% from **2**); white powder; mp 81–82 °C; $[\alpha]_D^{24}$ –69.0 (*c* = 1.11, $CHCl_3$).

IR (Nujol): 1744, 1614 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.21 (3 H, s), 1.22 (3 H, s), 1.41–1.50 (1 H, m), 1.88–2.15 (4 H, m), 2.21–2.32 (1 H, m), 2.46–2.56 (1 H, m), 2.98 (6 H, s).

^{13}C NMR ($CDCl_3$): δ = 20.9, 21.5, 27.1, 27.3, 43.3, 43.8, 50.6, 67.5, 168.8, 212.3.

MS (EI): *m/z* = 209 (M^+, 100).

Anal. Calcd for $C_{12}H_{19}NO_2$: C, 68.87; H, 9.15; N, 6.69. Found: C, 68.89; H, 9.19; N, 6.57.

(1*S*)-Diisobutylketopinamide (3b)
Yield: 77% from **2**; white powder; mp 91–93 °C; $[\alpha]_D^{26}$ +8.5 (*c* = 1.21, $CHCl_3$).

IR (Nujol): 1745, 1634 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.83–0.95 (12 H, m), 1.20 (3 H, s), 1.23 (3 H, s), 1.41–1.51 (1 H, m), 1.87–2.13 (6 H, m), 2.21–2.31 (1 H, m), 2.43–2.53 (1 H, m), 2.88 (1 H, dd, *J* = 7, 13 Hz), 3.09 (2 H, d, *J* = 8 Hz), 3.63 (1 H, dd, *J* = 8, 13 Hz).

^{13}C NMR ($CDCl_3$): δ = 19.7, 20.0, 20.3, 20.4, 21.3, 21.5, 25.7, 26.5, 27.4, 28.7, 42.9, 43.7, 50.9, 51.0, 54.1, 67.8, 169.4, 211.9.

MS (EI): *m*/*z* (%) = 293 (M^+, 18.4), 165 (100).

Anal. Calcd for $C_{18}H_{31}NO_2$: C, 73.67; H, 10.65; N, 4.77. Found: C, 73.45; H, 10.70; N, 4.52.

(1*S*)-Diisopropylketopinamide (3c)[6]
Yield: 73% from **2**; white powder; mp 126–127 °C; $[\alpha]_D^{24}$ –18.1 (*c* = 1.42, $CHCl_3$).

IR (Nujol): 1744, 1620 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.09 (3 H, d, *J* = 7 Hz), 1.21 (3 H, s), 1.22 (3 H, s), 1.29 (3 H, d, *J* = 7 Hz), 1.37 (3 H, d, *J* = 7 Hz), 1.40–1.48 (1 H, m), 1.45 (3 H, d, *J* = 7 Hz), 1.85–2.29 (5 H, m), 2.47 (1 H, ddd, *J* = 2, 5, 18 Hz), 3.35 (1 H, sept, *J* = 7 Hz), 3.89 (1 H, sept, *J* = 7 Hz).

^{13}C NMR ($CDCl_3$): δ = 20.4, 20.8, 20.9, 21.1, 21.4, 21.6, 27.1, 27.6, 43.2, 43.8, 46.4, 48.5, 50.9, 68.5, 167.7, 212.9.

MS (EI): *m*/*z* (%) = 265 (M^+, 15.4), 165 (100).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{27}NO_2$ (M^+): 265.2042; found: 265.2040.

1-[(1*S*)-Ketopinyl]pyrrolidine (3d)
Yield: 92% from **2**; white powder; mp 116–117 °C; $[\alpha]_D^{24}$ –46.7 (*c* = 1.09, $CHCl_3$).

IR (Nujol): 1744, 1609 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.19 (3 H, s), 1.25 (3 H, s), 1.40–1.49 (1 H, m), 1.70–1.75 (1 H, m), 1.87–2.13 (7 H, m), 2.19–2.30 (1 H, m), 2.46–2.55 (1 H, m), 3.16–3.25 (1 H, m), 3.49–3.53 (2 H, m), 3.70–3.77 (1 H, m).

^{13}C NMR ($CDCl_3$): δ = 20.6, 21.7, 23.5, 26.8, 26.8, 27.0, 43.5, 43.9, 46.8, 47.0, 50.1, 67.7, 167.7, 212.1.

MS (EI): *m*/*z* (%) = 235 (M^+, 8.3), 55 (100).

Anal. Calcd for $C_{14}H_{21}NO_2$: C, 71.46; H, 8.99; N, 5.95. Found: C, 71.67; H, 9.05; N, 5.96.

1-[(1*S*)-Ketopinyl]piperidine (3e)[14]
Yield: 90% from **2**; white powder; mp 93–94 °C; $[\alpha]_D^{24}$ –25.4 (*c* = 1.24, $CHCl_3$).

IR (Nujol): 1742, 1618 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.21 (3 H, s), 1.23 (3 H, s), 1.39–1.63 (7 H, m), 1.91 (1 H, d, *J* = 18 Hz), 2.24–2.34 (1 H, m), 2.49 (1 H, ddd, *J* = 3, 5, 18 Hz), 3.43 (4 H, br).

^{13}C NMR ($CDCl_3$): δ = 21.2, 21.4, 24.7, 27.1, 27.6, 43.2, 43.8, 50.6, 67.5, 167.1, 212.3.

MS (EI): *m*/*z* (%) = 249 (M^+, 27.4), 84 (100).

Anal. Calcd for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30; N, 5.62. Found: C, 72.30; H, 9.26; N, 5.52.

1-[(1*S*)-Ketopinyl]hexamethyleneimine (3f)
Yield: 96% from **2**; white powder; mp 90–91 °C; $[\alpha]_D^{24}$ –47.6 (*c* = 1.03, $CHCl_3$).

IR (Nujol): 1744, 1614 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.21 (3 H, s), 1.23 (3 H, s), 1.39–1.48 (2 H, m), 1.61–2.14 (11 H, m), 2.21–2.31 (1 H, m), 2.45–2.55 (1 H, m), 3.31–3.61 (4 H, m).

^{13}C NMR ($CDCl_3$): δ = 21.0, 21.7, 25.7, 27.0, 27.2, 27.8, 28.6, 30.1, 43.2, 43.9, 47.1, 47.7, 50.8, 67.9, 168.4, 212.4.

MS (EI): *m*/*z* (%) = 263 (M^+, 35.9), 98 (100).

Anal. Calcd for $C_{16}H_{25}NO_2$: C, 72.96; H, 9.57; N, 5.32. Found: C, 72.89; H, 9.66; N, 5.32.

1-[(1*S*)-Ketopinyl]heptamethyleneimine (3g)
Yield: 95% from **2**; white powder; mp 116–117 °C; $[\alpha]_D^{24}$ –41.5 (*c* = 1.50, $CHCl_3$).

IR (Nujol): 1732, 1614 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.22 (3 H, s), 1.23 (3 H, s), 1.41–1.97 (13 H, m), 2.04–2.14 (2 H, m), 2.22–2.32 (1 H, m), 2.49 (1 H, ddd, *J* = 2, 5, 18 Hz), 3.09–3.21 (2 H, m), 3.48–3.57 (1 H, m), 3.71–3.80 (1 H, m).

^{13}C NMR ($CDCl_3$): δ = 21.0, 21.6, 22.9, 25.9, 26.5, 27.2, 27.2, 27.6, 43.1, 43.8, 47.5, 50.0, 50.7, 67.9, 168.2, 212.4.

MS (EI): *m*/*z* (%) = 277 (M^+, 8.9), 112 (100).

Anal. Calcd for $C_{17}H_{27}NO_2$: C, 73.61; H, 9.81; N, 5.05. Found: C, 73.68; H, 9.90; N, 4.98.

4-[(1*S*)-Ketopinyl]morpholine (3h)
Yield: 83% from **2**; white powder; mp 117–119 °C; $[\alpha]_D^{24}$ –29.8 (*c* = 1.45, $CHCl_3$).

IR (Nujol): 1732, 1614 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.21 (3 H, s), 1.23 (3 H, s), 1.42–1.50 (1 H, m), 1.88–2.15 (4 H, m), 2.22–2.31 (1 H, m), 2.47–2.57 (1 H, m), 3.45–3.91 (4 H, br), 3.63–3.80 (4 H, m).

^{13}C NMR ($CDCl_3$): δ = 21.1, 21.4, 27.1, 27.3, 43.1, 43.7, 50.6, 67.1, 67.3, 167.5, 212.2.

MS (EI): *m*/*z* (%) = 251 (M^+, 60.6), 86 (100).

Anal. Calcd for $C_{14}H_{21}NO_3$: C, 66.91; H, 8.42; N, 5.57. Found: C, 66.70; H, 8.33; N, 5.47.

***cis*-2,6-Dimethyl-1-[(1*S*)-ketopinyl]piperidine (3i)**
Yield: 72% from **2**; white powder; mp 136 °C; $[\alpha]_D^{24}$ +19.3 (*c* = 1.05, $CHCl_3$).

IR (Nujol): 1732, 1614 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.21–1.24 (12 H, m), 1.41–2.09 (9 H, m), 2.24–2.32 (1 H, m), 2.48 (1 H, ddd, *J* = 2, 5, 18 Hz), 3.99 (2 H, m), 4.82 (2 H, m).

^{13}C NMR ($CDCl_3$): δ = 14.3, 20.9, 21.3, 21.7, 22.5, 27.3, 28.2, 30.1, 30.5, 42.9, 43.8, 44.2, 47.4, 51.1, 68.1, 167.5, 212.2.

MS (EI): *m*/*z* (%) = 277 (M^+, 33.2), 112 (100).

Anal. Calcd for $C_{17}H_{27}NO_2$: C, 73.61; H, 9.81; N, 5.05. Found: C, 73.50; H, 9.95; N, 4.96.

9-[(1*S*)-Ketopinyl]-9-azabicyclo[3.3.1]nonane (3j)
Yield: 93% from **2**; white powder; mp 182–183 °C; $[\alpha]_D^{26}$ –0.8 (*c* = 0.65, $CHCl_3$).

IR (Nujol): 1742, 1605 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.23 (3 H, s), 1.24 (3 H, s), 1.38–1.48 (1 H, m), 1.58–2.14 (15 H, m), 2.21–2.37 (2 H, m), 2.43–2.53 (1 H, m), 3.87 (1 H, br), 4.78 (1 H, br).

^{13}C NMR ($CDCl_3$): δ = 19.8, 19.9, 21.3, 21.5, 27.3, 27.7, 29.4, 29.9, 30.5, 30.8, 43.3, 43.7, 43.8, 49.0, 50.7, 67.7, 166.1, 212.3.

MS (EI): *m*/*z* (%) = 289 (M^+, 59.5), 165 (100).

Anal. Calcd for $C_{18}H_{27}NO_2$: C, 74.70; H, 9.40; N, 4.84. Found: C, 74.42; H, 9.34; N, 5.08.

γ-Amino Alcohol 1; (1*R*,2*R*)-10-(Dimethylamino)isoborneol (1a); Typical Procedure

$LiAlH_4$ (109 mg, 2.87 mmol) was added to a solution of **3a** (300 mg, 1.43 mmol) in THF (6 ml) at 0 °C under argon. The mixture was stirred for 0.5 h at r.t. and then refluxed for 2 h. After adding $Na_2SO_4{\cdot}10H_2O$ at 0 °C, the mixture was filtered. The filtrate was concentrated in vacuo and the residue was purified by flash column chromatography (EtOAc–MeOH, 1:1) to give **1a** (260 mg, 92%); colorless oil; $[\alpha]_D^{25}$ –75.3 (*c* = 0.61, $CHCl_3$).

IR (neat): 3416, 2951, 2878, 1454 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.79 (3 H, s), 0.99–1.09 (1 H, m), 1.14 (3 H, s), 1.30–1.40 (1 H, m), 1.45–1.56 (1 H, m), 1.64–1.86 (4 H, m), 2.11, 2.79 (2 H, AB, *J* = 13 Hz), 2.28 (6 H, s), 3.98 (1 H, dd, *J* = 4, 8 Hz), 5.15 (1 H, br).

MS (EI): *m*/*z* = 197 (M^+, 14.0), 45 (100).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{23}NO$ (M^+): 197.1780; found: 197.1795.

(1*R*,2*R*)-10-(Diisobutylamino)isoborneol (1b)

Yield: 93%; colorless oil; $[\alpha]_D^{25}$ –147.6 (*c* = 0.88, $CHCl_3$).

IR (neat): 3383, 2953, 2804, 1468 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.80 (3 H, s), 0.87 (6 H, d, *J* = 7 Hz), 0.98 (6 H, d, *J* = 7 Hz), 1.01–1.09 (1 H, m), 1.15 (3 H, s), 1.32–1.42 (1 H, m), 1.47–1.57 (1 H, m), 1.64–1.87 (6 H, m), 1.94 (2 H, dd, *J* = 3, 13 Hz), 2.09, 2.89 (2 H, AB, *J* = 13 Hz), 2.30 (2 H, dd, *J* = 10, 13 Hz), 3.95 (1 H, dd, *J* = 4, 8 Hz), 5.38 (1 H, s).

^{13}C NMR ($CDCl_3$): δ = 20.5, 20.6, 21.0, 21.7, 26.3, 27.9, 34.8, 39.0, 44.6, 48.5, 50.7, 56.9, 65.4, 77.6.

MS (EI): *m*/*z* 281 (M^+, 5.7), 86 (100).

Anal. Calcd for $C_{18}H_{35}NO$: C, 76.81; H, 12.53; N, 4.98. Found: C, 76.58; H, 12.65; N, 4.94.

(1*R*,2*R*)-10-(Diisopropylamino)isoborneol (1c)[6]

Yield: 95%; white powder; mp 69–71 °C; $[\alpha]_D^{24}$ –68.6 (*c* = 1.48, $CHCl_3$).

IR (neat): 3344 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.84 (3 H, s), 0.99 (6 H, d, *J* = 7 Hz), 1.00–1.08 (1 H, m), 1.09 (6 H, d, *J* = 7 Hz), 1.19 (3 H, s), 1.29–1.37 (1 H, m), 1.47–1.57 (1 H, m), 1.64–1.83 (4 H, m), 2.56, 2.78 (2 H, AB, *J* = 14 Hz), 3.14 (2 H, sept, *J* = 7 Hz), 3.93 (1 H, dd, *J* = 4, 8 Hz), 6.01 (1 H, br).

^{13}C NMR ($CDCl_3$): δ = 17.3, 20.5, 20.7, 22.5, 27.9, 35.0, 39.3, 44.0, 44.5, 47.9, 48.6, 50.0, 78.1.

MS (EI): *m*/*z* 253 (M^+, 8.0), 238 (100).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{31}NO$ (M^+): 253.2406; found: 253.2408.

(1*R*,2*R*)-10-Pyrrolidinoisoborneol (1d)

Yield: 92%; colorless oil; $[\alpha]_D^{25}$ –75.7 (*c* = 1.18, $CHCl_3$).

IR (neat): 3416, 2953, 2878, 2800 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.81 (3 H, s), 1.01–1.08 (1 H, m), 1.14 (3 H, s), 1.27–1.36 (1 H, m), 1.44–1.55 (1 H, m), 1.63–1.84 (8 H, m), 2.14, 3.11 (2 H, AB, *J* = 13 Hz), 2.48–2.51 (2 H, m), 2.63–2.66 (2 H, m), 3.94 (1 H, dd, *J* = 4, 8 Hz), 5.06 (1 H, br).

^{13}C NMR ($CDCl_3$): δ = 20.4, 20.6, 23.9, 27.5, 33.4, 38.9, 44.9, 47.5, 51.2, 55.8, 55.9, 78.4.

MS (EI): *m*/*z* (%) = 223 (M^+, 71.4), 41 (100).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{25}NO$ (M^+): 223.1936; found: 223.1907.

(1*R*,2*R*)-10-Piperidinoisoborneol (1e)

Yield: 96%; colorless oil; $[\alpha]_D^{26}$ –68.0 (*c* = 1.12, $CHCl_3$).

IR (neat): 3383, 2934, 2878, 2806 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.80 (3 H, s), 0.97–1.07 (1 H, m), 1.15 (3 H, s), 1.25–1.71 (11 H, m), 1.77–1.85 (1 H, m), 2.25, 2.70 (2 H, AB, *J* = 13 Hz), 2.35 (2 H, br), 2.57 (2 H, br), 3.96 (1 H, dd, *J* = 4, 8 Hz), 5.78 (1 H, br).

^{13}C NMR ($CDCl_3$): δ = 20.5, 24.0, 26.3, 27.8, 34.4, 39.2, 44.8, 47.9, 50.7, 56.1, 59.5, 78.4.

MS (EI): *m*/*z* (%) = 237 (M^+, 44.8), 84 (100).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{27}NO$ (M^+): 237.2093; found: 237.2087.

(1*R*,2*R*)-10-(Hexamethyleneimino)isoborneol (1f)

Yield: 97%; colorless amorphous solid; mp <30 °C; $[\alpha]_D^{26}$ –44.4 (*c* = 1.09, $CHCl_3$).

IR (neat): 3317, 2924, 1475, 1360 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.79 (3 H, s), 0.98–1.08 (1 H, m), 1.15 (3 H, s), 1.29–1.38 (1 H, m), 1.44–1.74 (12 H, m), 1.78–1.87 (1 H, m), 2.54, 2.73 (2 H, AB, *J* = 13 Hz), 2.57–2.64 (2 H, m), 2.68–2.75 (2 H, m), 3.95 (1 H, dd, *J* = 4, 8 Hz), 5.86 (1 H, br).

^{13}C NMR ($CDCl_3$): δ = 20.5, 26.9, 27.7, 28.4, 34.1, 39.1, 44.7, 47.9, 51.0, 57.2, 59.2, 78.6.

MS (EI): *m*/*z* = 251 (M^+, 64.2), 70 (100).

Anal. Calcd for $C_{16}H_{29}NO$: C, 76.44; H, 11.63; N, 5.57. Found: C, 76.22; H, 11.68; N, 5.50.

(1*R*,2*R*)-10-(Heptamethyleneimino)isoborneol (1g)

Yield: 93%; white powder; mp 36–38 °C; $[\alpha]_D^{26}$ –48.4 (*c* = 1.04, $CHCl_3$).

IR (Nujol): 3420 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.79 (3 H, s), 1.00–1.09 (1 H, m), 1.14 (3 H, s), 1.31–1.40 (1 H, m), 1.45–1.75 (14 H, m), 1.78–1.85 (1 H, m), 2.41, 2.74 (2 H, AB, *J* = 13 Hz), 2.48–2.69 (4 H, m), 3.98 (1 H, dd, *J* = 4, 8 Hz), 5.06 (1 H, br).

^{13}C NMR ($CDCl_3$): δ = 20.5, 20.6, 25.6, 27.5, 27.7, 33.4, 38.8, 44.7, 48.0, 51.3, 56.8, 60.2, 78.2.

MS (EI): *m*/*z* 265 (M^+, 27.1), 126 (100).

Anal. Calcd for $C_{17}H_{31}NO$: C, 76.92; H, 11.77; N, 5.28. Found: C, 76.65; H, 11.80; N, 5.11.

(1*R*,2*R*)-10-Morpholinoisoborneol (1h)

Yield: 99%; white powder; mp 42–43 °C; $[\alpha]_D^{26}$ –75.8 (*c* = 1.04, $CHCl_3$).

IR (neat): 3404, 2922, 1454, 1377 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.81 (3 H, s), 1.00–1.09 (1 H, m), 1.14 (3 H, s), 1.24–1.34 (1 H, m), 1.49–1.60 (1 H, m), 1.65–1.87 (4 H, m), 2.29, 2.75 (2 H, AB, *J* = 13 Hz), 2.39–2.47 (2 H, m), 2.63–2.67 (2 H, m), 3.71 (4 H, dd, *J* = 5, 5 Hz), 3.95 (1 H, dd, *J* = 4, 8 Hz), 4.78 (1 H, br).

^{13}C NMR ($CDCl_3$): δ = 20.4, 20.5, 27.7, 34.1, 39.0, 44.7, 48.0, 50.9, 55.2, 59.3, 67.0, 78.1.

MS (EI): *m*/*z* 239 (M^+, 44.7), 87 (100).

Anal. Calcd for $C_{14}H_{25}NO_2$: C, 70.25; H, 10.53; N, 5.85. Found: C, 70.17; H, 10.72; N, 5.65.

(1*R*,2*R*)-10-(*cis*-2,6-Dimethylpiperidino)isoborneol (1i)
Yield: 97%; white powder; mp 83–85 °C; $[\alpha]_D^{24}$ –43.3 (*c* = 1.13, $CHCl_3$).

IR (Nujol): 3285 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.83 (3 H, s), 0.95–1.05 (1 H, m), 1.09 (3 H, d, *J* = 7 Hz), 1.09 (3 H, d, *J* = 7 Hz), 1.18 (3 H, s), 1.26–1.73 (11 H, m), 1.75–1.84 (1 H, m), 2.67, 2.82 (2 H, AB, *J* = 14 Hz), 2.86 (1 H, br), 3.07 (1 H, br), 3.97 (1 H, dd, *J* = 4, 8 Hz), 6.17 (1 H, br).

^{13}C NMR ($CDCl_3$): δ = 15.8, 16.8, 17.8, 20.7, 20.8, 27.7, 31.4, 31.5, 34.3, 39.5, 44.9, 48.2, 50.6, 52.1, 52.4, 55.6, 78.7.

MS (EI): *m*/*z* (%) = 265 (M^+, 9.2), 250 (100).

Anal. Calcd for $C_{17}H_{31}NO$: C, 76.92; H, 11.77; N, 5.28. Found: C, 76.71; H, 11.84; N, 5.29.

(1*R*,2*R*)-10-(9-Azabicyclo[3.3.1]nonan-9-yl)isoborneol (1j)
Yield: 96%; white powder; mp 155–157 °C; $[\alpha]_D^{24}$ –35.2 (*c* = 0.91, $CHCl_3$).

IR (Nujol): 3381 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.83 (3 H, s), 0.95–1.05 (1 H, m), 1.17–1.26 (1 H, m), 1.18 (3 H, s), 1.45–1.73 (10 H, m), 1.77–2.06 (7 H, m), 2.64, 3.10 (2 H, AB, *J* = 14 Hz), 2.90 (2 H, br), 3.94 (1 H, dd, *J* = 4, 8 Hz), 6.42 (1 H, br).

^{13}C NMR ($CDCl_3$): δ = 20.5, 20.7, 20.8, 27.6, 34.0, 39.5, 45.1, 47.6, 50.8, 53.2, 78.6.

MS (EI): *m*/*z* = 277 (M^+, 42.7), 125 (100).

Anal. Calcd for $C_{18}H_{31}NO$: C, 77.92; H, 11.26; N, 5.05. Found: C, 78.03; H, 11.33; N, 4.81.

Asymmetric Addition of Diethylzinc to Aldehydes; General Procedure
Diethylzinc (1.0 M in hexane, 2 mL, 2.0 mmol) was added to ligand **1** (0.050 mmol) in the solvent (2 mL) given in Table 1 under argon and the mixture was stirred for 0.5 h at r.t. After the addition of aldehyde (1.0 mmol) at 0 °C, the mixture was stirred at r.t. and aq 1 N HCl was added at 0 °C. After usual work-up, pure alcohols were obtained by flash column chromatography. The enantiomeric excess and the absolute configuration of the resulting alcohol were determined by using HPLC and the optical rotation, respectively.

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