Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron: Asymmetry
Tetrahedron: *Asymmetry* 17 (2006) 1663–1670

Synthesis of chiral ligands containing the *N*-(*S*)-α-phenylethyl group and their evaluation as activators in the enantioselective addition of Et_2Zn to benzaldehyde

Virginia M. Mastranzo,[a,b] Ericka Santacruz,[a,b] Gabriela Huelgas,[a,b] Evelyn Paz,[b] Martha V. Sosa-Rivadeneyra,[b] Sylvain Bernès,[b] Eusebio Juaristi,[c,*] Leticia Quintero[b,*] and Cecilia Anaya de Parrodi[a,*]

[a]*Universidad de las Américas Puebla, Departamento de Ciencias Químico-Biológicas, Santa Catarina Mártir s/n, Cholula, Puebla 72820, Mexico*
[b]*Centro de Investigación de la Facultad de Ciencias Químicas, Universidad Autónoma de Puebla, 72570 Puebla, Mexico*
[c]*Centro de Investigación y de Estudios Avanzados del Instituto Politécnico Nacional, Departamento de Química, México, DF 07000, Mexico*

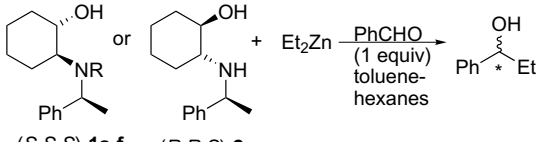
Received 20 April 2006; accepted 5 June 2006

Abstract—The synthesis of chiral ligands **4**–**18** derived from *N*-[(*S*)-α-phenylethyl]-*trans*-β-aminocyclohexanols (*S*,*S*,*S*)-**1a** and (*R*,*R*,*S*)-**2** is described. Addition of diethylzinc to benzaldehyde catalyzed by ligands **4**–**18** (6 mol %) proceeds in fair to good yield (45–86%), and low to good enantioselectivities (1–76% ee). Highest enantioselectivities were induced by ligands (*S*,*S*,*S*)-**4** and (*S*,*S*,*S*,*S*,*R*,*R*)-**18** (76% and 68% ee, respectively). The configuration of the major enantiomer of carbinol **3** is (*R*) in both cases.

1. Introduction

The asymmetric addition of dialkylzinc to aldehydes has become a standard test in the design of new ligands for catalytic enantioselective synthesis.[1–7] Indeed, the chiral alcohols that are produced in this reaction are ubiquitous in Nature and in many drugs. Furthermore, they are important precursors to many other organic molecules of relevance. The application of the (*S*)-α-phenylethyl group as chiral auxiliary has proven quite effective in asymmetric synthesis.[8,9] Recently, ligands containing *trans*-β-aminocyclohexanol[10,11] and *trans*-1,2-diaminocyclohexane[12] cores have been reported as effective constituents of catalysts in the enantioselective addition of diethylzinc to aldehydes. There are also some examples in the literature of the use of chiral oxazolidines[13] and imidazolidines,[14] derived from β-aminoalcohols and 1,2-diamines as catalysts.

Our group has reported the asymmetric addition of diethylzinc to benzaldehyde in the presence of *N*-(alkylated)-*N*-[(*S*)-α-phenylethyl]-β-aminocyclohexanols (*S*,*S*,*S*)-**1a**–**f** to give (*R*)-**3** in 81–90% isolated yield and 57–76% ee. By contrast the diastereomeric (*R*,*R*,*S*)-**2** ligand gave (*S*)-**3** in 50% ee (Scheme 1).[11]



β-Aminoalcohol	R	% ee[a]
(*S*,*S*,*S*)-**1a**	H	57 (*R*)
(*S*,*S*,*S*)-**1b**	Me	65 (*R*)
(*S*,*S*,*S*)-**1c**	Et	73 (*R*)
(*S*,*S*,*S*)-**1d**	Pr	76 (*R*)
(*S*,*S*,*S*)-**1e**	Bu	75 (*R*)
(*S*,*S*,*S*)-**1f**	Pent	68 (*R*)
(*R*,*R*,*S*)-**2**	H	50 (*S*)

[a]Configuration of major product.

Scheme 1.

* Corresponding authors. E-mail: cecilia.anaya@udlap.mx

0957-4166/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2006.06.005

Herein, we report the synthesis of related ligands **4**–**18** containing multiple stereogenic centers. These ligands were prepared from *trans*-*N*-[(*S*)-α-phenylethyl]-β-aminocyclohexanols (*S*,*S*,*S*)-**1a** and (*R*,*R*,*S*)-**2** (Chart 1). We also evaluated the potential of these chiral ligands as catalysts in the enantioselective addition of diethylzinc to benzaldehyde.

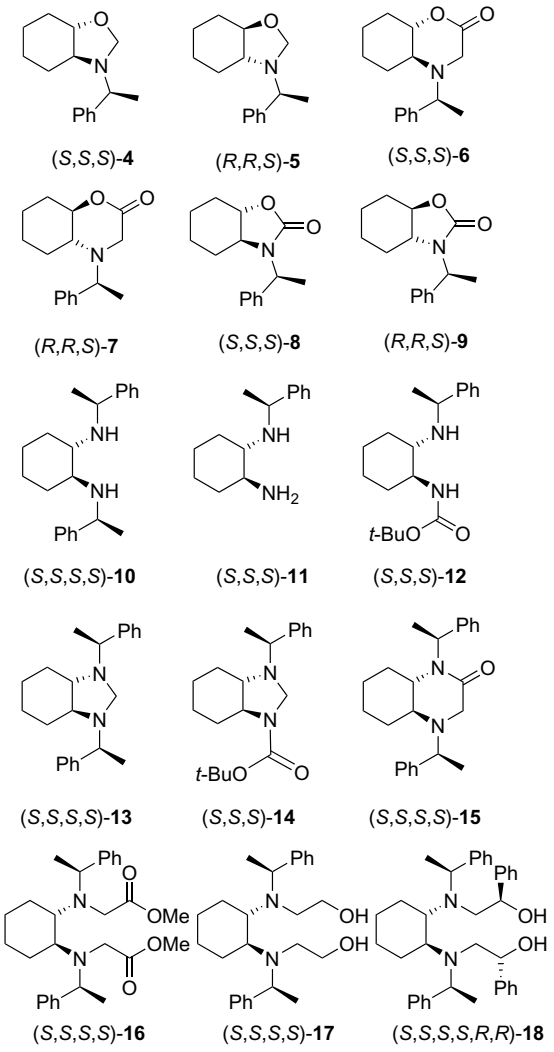
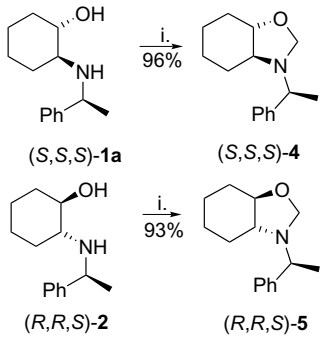


Chart 1.

2. Results and discussion

2.1. Synthesis of *N*-[(*S*)-α-phenylethyl]-*trans*-β-aminocyclohexanols derivatives 4–9

N-[(*S*)-α-Phenylethyl]-β-aminocyclohexanols (*S*,*S*,*S*)-**1a** and (*R*,*R*,*S*)-**2** were prepared from cyclohexene oxide and (*S*)-α-phenylethylamine as described in the literature.[10,11] Both aminoalcohols (*S*,*S*,*S*)-**1a** and (*R*,*R*,*S*)-**2** (1 equiv) were treated separately with paraformaldehyde (6 equiv) in toluene and heated to reflux for 1.5 h, to afford (3a*S*,7a*S*)- and (3a*R*,7a*R*)-3-[(*S*)-α-phenylethyl]-octahydrobenzo[*d*]oxazoles (*S*,*S*,*S*)-**4** and (*R*,*R*,*S*)-**5** (96% and 93% yield, respectively, Scheme 2). Figure 1 shows the computer-generated X-ray diffraction structure of oxazole (*S*,*S*,*S*)-**4**, which shows *like* relative configurations between stereocenters at C(3a) and C(7a) and the known (*S*)-configured α-phenylethylamino group.



Scheme 2. Reagents and conditions: (i) excess $(CH_2O)_n$, toluene, reflux, 1.5 h.

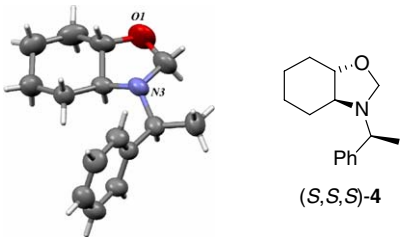
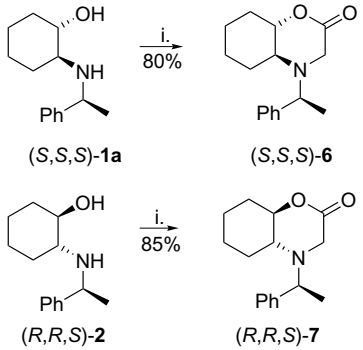


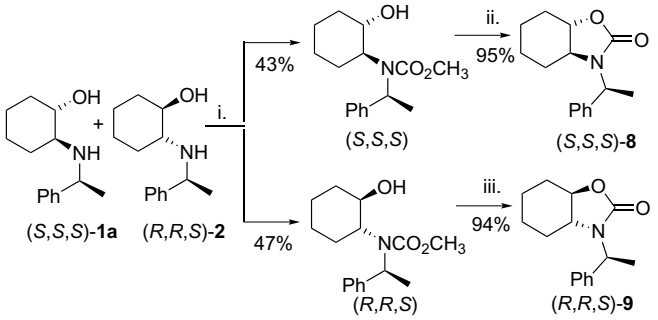
Figure 1. Computer-generated structure of (3a*S*,7a*S*)-3-[(*S*)-α-phenylethyl]-octahydrobenzo[*d*]oxazole **4** based upon the X-ray diffraction data.

The 4-oxazin-2-ones (*S*,*S*,*S*)-**6** and (*R*,*R*,*S*)-**7** were prepared separately from (*S*,*S*,*S*)-**1a** and (*R*,*R*,*S*)-**2** (1 equiv) in the presence of glyoxal (40% aqueous solution v/v), following the procedure described in the literature (Scheme 3).[15]



Scheme 3. Reagents and conditions: (i) OHCCHO 40% aq/THF/rt, 2 h.

The oxazolidin-2-ones (*S*,*S*,*S*)-**8** and (*R*,*R*,*S*)-**9** were prepared following the procedure described in the literature,[16] with (*S*,*S*,*S*)-**1a** and (*R*,*R*,*S*)-**2** in the presence of methyl chloroformate and NaH in THF by heating to reflux for 2.5 h (Scheme 4). The intermediate (*S*,*S*,*S*)- and (*R*,*R*,*S*)-carbamates were separated by column chromatography



Scheme 4. Reagents and conditions: (i) (1) $ClCO_2Me$, NaH, THF, reflux, 2.5 h; (2) column chromatography; (ii) NaH, THF, reflux, 6 h; (iii) NaH, THF, reflux, 4.5 h.

on silica gel [hexanes–EtOAc (5:1)], in 43% and 47%, respectively. Next, the (*S*,*S*,*S*)- and (*R*,*R*,*S*)-carbamates were cyclized under basic conditions by treatment with NaH in THF under reflux, for 4.5 and 6 h, respectively, to give the desired oxazolidinones (*S*,*S*,*S*)-**8** and (*R*,*R*,*S*)-**9** (95% and 94% yield).

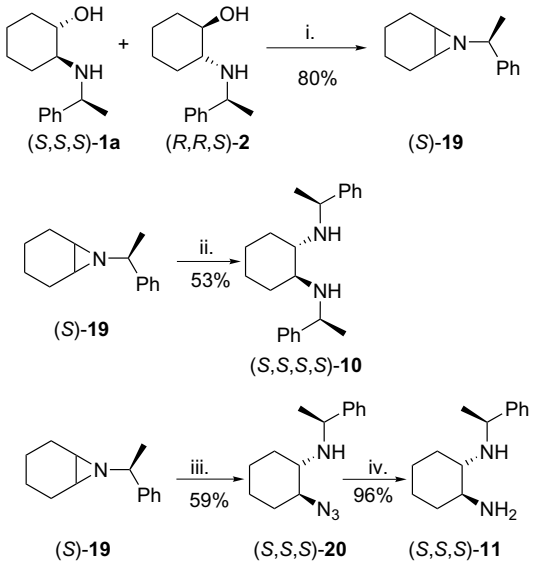
2.2. Synthesis of *N*,*N*′-di[(*S*)-α-phenylethyl]- and *N*-[(*S*)-α-phenylethyl]-*trans*-1,2-cyclohexanediamine derivatives 10–18

As part of an ongoing project involving chiral diamines containing the *trans*-1,2-diaminocyclohexane core,[17] we decided to prepare several ligands derived from β-amino-alcohol (*S*,*S*,*S*)-**1a** (Chart 1).

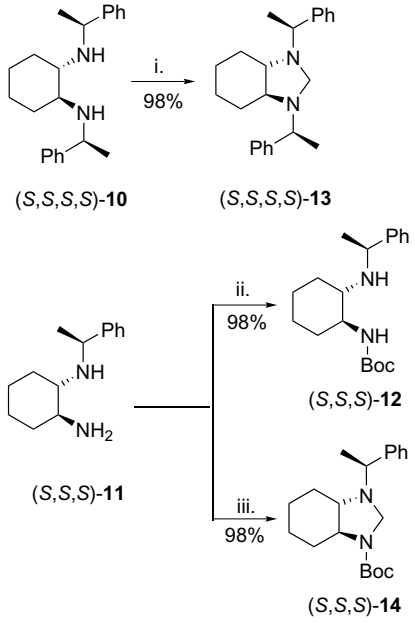
N-(*S*)-(α-Phenylethyl)cyclohexene aziridine (*S*)-**19** was used as the starting material for the synthesis of *trans*-1,2-cyclohexanediamines (*S*,*S*,*S*,*S*)-**10** and (*S*,*S*,*S*)-**11**. Aziridine (*S*)-**19** was prepared from the diastereoisomeric mixture of β-aminoalcohols (*S*,*S*,*S*)-**1a** and (*R*,*R*,*S*)-**2** by mesylation of the hydroxyl group followed by spontaneous intramolecular nucleophilic substitution (S_N2). The reaction was performed following the procedure described in the literature (Scheme 5).[17]

Diamine (*S*,*S*,*S*,*S*)-**10** was prepared by aminolysis of (*S*)-**19** in the presence of (*S*)-α-phenylethylamine, 1 equiv of lithium perchlorate as activator and acetonitrile as solvent at reflux, as previously reported (Scheme 5).[17] Diastereomer (*S*,*S*,*S*,*S*)-**10** was the major product (ca. 67% ds) and was separated by column chromatography on deactivated silica gel [$Et_3N/SiO_2 = 2.5\%$ v/v, hexanes–EtOAc (30:1)] in 53% yield. The ring opening of aziridine (*S*)-**19** by ring opening with sodium azide catalyzed by $CeCl_3{\cdot}7H_2O$ (0.5 equiv) in CH_3CN–H_2O (9:1) was also stereoselective affording amines (*S*,*S*,*S*)-**20** and (*R*,*R*,*S*)-**20** in ca. 2:1 ratio.[18] The major product *trans*-(*S*,*S*,*S*)-2-azido amine was purified by column chromatography on deactivated silica gel [$Et_3N/SiO_2 = 2.5\%$ v/v, hexanes–EtOAc (30:1)] in 59% yield. Reduction of the major diastereomer (*S*,*S*,*S*)-**20** under a hydrogen atmosphere in the presence of 10% palladium hydroxide on carbon as catalyst afforded diamine (*S*,*S*,*S*)-**11** in 96% yield (Scheme 5).

The addition of di-*tert*-butyl dicarbonate to diamine (*S*,*S*,*S*)-**11**, followed by stirring for 24 h, afforded the *N*-Boc protected amine (*S*,*S*,*S*)-**12** (Scheme 6). The reaction of diamine (*S*,*S*,*S*,*S*)-**10** with formaldehyde (37% aqueous solution v/v) took place in 2 h, in the presence of K_2CO_3 (2.5 equiv) and $MgSO_4$ (3.0 equiv), using $CHCl_3$ as solvent affording the imidazolidine (*S*,*S*,*S*)-**13**. By the same token, (*S*,*S*,*S*)-**11** leads to the *N*-Boc protected imidazolidine (*S*,*S*,*S*)-**14** (Scheme 6).

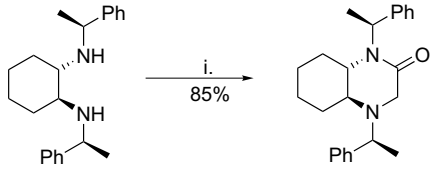


Scheme 5. Reagents and conditions: (i) MsCl, Et_3N, THF, rt, 48 h; (ii) (*S*)-H_2NCHCH_3Ph, $LiClO_4$, CH_3CN, reflux; column chromatography; (iii) NaN_3, CH_3CN–H_2O (9:1), $CeCl_3{\cdot}7H_2O$, 3 h; (iv) (1) $H_2/Pd(OH)_2/C$ 10%; (2) column chromatography.



Scheme 6. Reagents and conditions: (i) $K_2CO_3/MgSO_4/CHCl_3$, CH_2O–H_2O (37% v/v); (ii) $(Boc)_2O$; (iii) (1) $K_2CO_3/MgSO_4/CHCl_3$, CH_2O–H_2O (37% v/v); (2) $(Boc)_2O$.

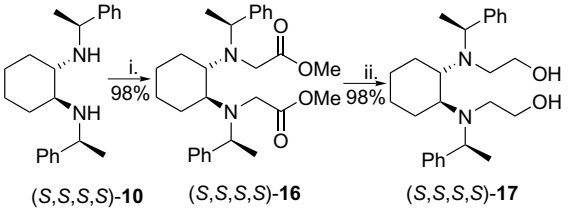
Ligand (*S*,*S*,*S*,*S*)-**15** was prepared from diamine (*S*,*S*,*S*,*S*)-**10** and glyoxal according to the same procedure as described for the synthesis of 4-oxazin-2-ones (*S*,*S*,*S*)-**6** and (*R*,*R*,*S*)-**7** (Scheme 7).[15]



(*S*,*S*,*S*,*S*)-**10** (*S*,*S*,*S*,*S*)-**15**

Scheme 7. Reagents and conditions: (i) OHCCHO 40% aq, CH_2Cl_2, rt, 2 h.

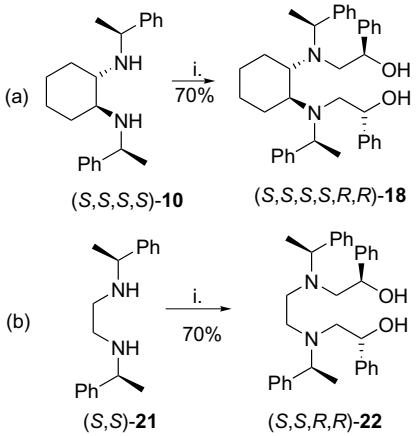
The C_2-symmetric 1,2-diamine (*S*,*S*,*S*,*S*)-**10** was also used as the starting material for the synthesis of tetradentated ligands. In particular, dialkylation of diamine (*S*,*S*,*S*,*S*)-**10** in the presence of 2 equiv of methyl bromoacetate afforded compound (*S*,*S*,*S*,*S*)-**16** (98% yield). Reduction of (*S*,*S*,*S*,*S*)-**16** with $LiAlH_4$ in THF at room temperature gave diol (*S*,*S*,*S*,*S*)-**17** in an excellent 98% yield (Scheme 8).



(*S*,*S*,*S*,*S*)-**10** (*S*,*S*,*S*,*S*)-**16** (*S*,*S*,*S*,*S*)-**17**

Scheme 8. Reagents and conditions: (i) $BrCH_2COOMe/K_2CO_3/CH_3CN$; (ii) $LiAlH_4$, THF, rt, 2 h.

β-Aminoalcohol (*S*,*S*,*S*,*S*,*R*,*R*)-**18** and its open chain analogue (*S*,*S*,*R*,*R*)-**22** were prepared from the corresponding diamines (*S*,*S*,*S*,*S*)-**10** and 1,2-bis-[(*S*)-α-phenylethyl]-ethylenediamine (*S*,*S*)-**21**,[19] by aminolysis of (*R*)-styrene oxide (2 equiv), in the presence of $LiClO_4$ (2 equiv) in acetonitrile at reflux. Both reactions proceeded in 70% yield (Scheme 9).



(*S*,*S*,*S*,*S*)-**10** (*S*,*S*,*S*,*S*,*R*,*R*)-**18**

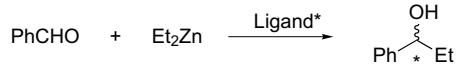
(*S*,*S*)-**21** (*S*,*S*,*R*,*R*)-**22**

Scheme 9. Reagents and conditions: (i) (*R*)-styrene oxide (2.0 equiv)/$LiClO_4$ (2.0 equiv)/CH_3CN.

2.3. Enantioselective addition of diethylzinc to benzaldehyde

The asymmetric addition reaction of diethylzinc (2.03 equiv) to benzaldehyde (1.0 equiv) using 6 mol % of chiral ligands **4**–**18** containing the *trans*-β-aminocyclohexanol moiety (Table 1, entries 1–6), and *trans*-1,2-diaminocyclohexane core (Table 1, entries 7–15) afforded carbinol **3** with satisfactory yields (45–86%), and low to good enantioselectivities (1–76% ee; Table 1).

Table 1. Enantioselective ethylation of benzaldehyde



1.0 equiv 2.03 equiv 0.06 equiv **3**

Entry	Ligand[a]	% ee (yield, %)[b]	Predominant configuration[c]
1	(*S*,*S*,*S*)-**4**	76 (79)	(*R*)
2	(*R*,*R*,*S*)-**5**	25 (80)	(*S*)
3	(*S*,*S*,*S*)-**6**	18 (75)	(*S*)
4	(*R*,*R*,*S*)-**7**	57 (86)	(*R*)
5	(*S*,*S*,*S*)-**8**	2 (78)	(*R*)
6	(*R*,*R*,*S*)-**9**	7 (75)	(*S*)
7	(*S*,*S*,*S*,*S*)-**10**	3 (75)	(*S*)
8	(*S*,*S*,*S*)-**11**	5 (50)	(*S*)
9	(*S*,*S*,*S*)-**12**	44 (60)	(*R*)
10	(*S*,*S*,*S*)-**13**	9 (55)	(*R*)
11	(*S*,*S*,*S*)-**14**	4 (46)	(*S*)
12	(*S*,*S*,*S*,*S*)-**15**	1 (45)	(*R*)
13	(*S*,*S*,*S*,*S*)-**16**	7 (54)	(*S*)
14	(*S*,*S*,*S*,*S*)-**17**	10 (65)	(*R*)
15	(*S*,*S*,*S*,*S*,*R*,*R*)-**18**	68 (70)	(*R*)
16	(*S*,*S*,*R*,*R*)-**22**	37 (65)	(*R*)

[a] All reactions were performed using 6 mol % of the chiral ligand.

[b] The analyses for determining enantiomeric excess were performed after purification by column chromatography on deactivated silica gel ($Et_3N/SiO_2 = 2.5\%$ v/v, hexanes–EtOAc, 94:6) by HPLC using a Chiralcel OD column under conditions reported previously.

[c] Optical rotations were measured and compared with those reported in the literature.[11]

Most reports on the catalyzed addition of dialkylzinc to aldehydes use β-aminoalcohols as ligands.[3–7] The three novel β-aminoalcohols prepared in this work [(*S*,*S*,*S*,*S*)-**17**, (*S*,*S*,*S*,*S*,*R*,*R*)-**18**, and (*S*,*S*,*R*,*R*)-**22**] do activate diethylzinc for efficient addition to benzaldehyde (65–70% yield). On the other hand, some examples of activation with diamine ligands have been reported.[12,20] Disappointingly, the diamines examined in this work (**10**–**16**, entries 7–13 in Table 1) did promote the addition of diethylzinc to benzaldehyde but with quite low enantioinduction (1–44% ee).

The highest enantioselectivities were observed with β-aminoalcohol (*S*,*S*,*S*,*S*,*R*,*R*)-**18** (68% ee) and with oxazolidine (*S*,*S*,*S*)-**4** (76% ee). Interestingly, (*R*,*R*,*S*)-**5**, which is diastereomer of (*S*,*S*,*S*)-**4** appears to present a mismatched combination of stereogenic centers[21] since carbinol (*S*)-**3** is produced in a poor 25% ee. Several groups have reported the effectiveness of chiral oxazolidines as catalysts in the enantioselective addition of diethylzinc to aromatic and aliphatic aldehydes.[13] In the present study, partial hydrolysis (10–15%) of oxazolidines (*S*,*S*,*S*)-**4** and (*R*,*R*,*S*)-**5** was ob-

served under the reaction conditions; nevertheless, the observed enantiomeric ratios of (*R*)- and (*S*)-**3** (Table 1) seem to originate from oxazolidine rather than β-aminoalcohol catalysis (compare with ee values reported in Scheme 1). Thus, it seems that for oxazolidines (*S*,*S*,*S*)-**4** and (*R*,*R*,*S*)-**5** the α-phenylethyl substituent does not play an important role on the stereochemical outcome—apparently the stereocenter at C(3a) plays this role.

3. Conclusions

Chiral ligands **4**–**18** were prepared from cyclohexene oxide in good yields. These chiral ligands were examined as catalysts in the enantioselective addition of Et_2Zn to benzaldehyde. Best results (highest enantioinduction) were found with (*S*,*S*,*S*)-**4** and (*S*,*S*,*S*,*S*,*R*,*R*)-**18**. On the other hand, 1,2-diamines (*S*,*S*,*S*,*S*)-**10** and (*S*,*S*,*S*,*S*)-**11** showed very poor enantioselection compared with the analogous β-aminoalcohol (*S*,*S*,*S*)-**1a**. By contrast, it was observed that oxazolidine (*S*,*S*,*S*)-**4** afforded higher enantioselectivities than the corresponding imidazolidines (*S*,*S*,*S*,*S*)-**12** and (*S*,*S*,*S*,*S*)-**14**. The same behavior was observed with the 4-oxazin-2-ones (*S*,*S*,*S*)-**6** and (*R*,*R*,*S*)-**7**, compared with oxazolidin-2-ones (*S*,*S*,*S*)-**8**, (*R*,*R*,*S*)-**9**, and piperazin-2-one (*S*,*S*,*S*)-**15**. Furthermore, the introduction of additional coordinating sites in the ligand, and the presence of multiple stereogenic centers as in the case of diamino diol (*S*,*S*,*S*,*S*,*R*,*R*)-**18** led to improved enantioselectivity. Finally, comparing ligand (*S*,*S*,*S*,*S*,*R*,*R*)-**18** with (*S*,*S*,*R*,*R*)-**22** we observed that the presence of the cyclohexane core gave better enantioselection, presumably owing to a more rigid transition state for the addition reaction in the former ligand.

4. Experimental

4.1. General methods

All manipulations involving diethylzinc were carried out under an argon atmosphere. Benzaldehyde was distilled prior to use. NMR spectra were obtained on 200, 300, and 400 MHz Fourier transform spectrometers. ^{1}H NMR spectra were referenced to tetramethylsilane; $^{13}C\{^1H\}$ NMR spectra were referenced to residual $CHCl_3$.

4.2. (1*S*,2*S*)- and (1*R*,2*R*)-1-*N*-[(*S*)-α-Phenylethyl]-β-aminocyclohexanol, (*S*,*S*,*S*)-1a and (*R*,*R*,*S*)-2

These β-aminoalcohols were prepared from cyclohexene oxide and (*S*)-α-phenylethylamine according to the literature procedure.[10,11]

4.3. General procedure for the preparation of octahydrobenzo[*d*]oxazoles

A solution of β-aminoalcohol (*S*,*S*,*S*)-**1a** or (*R*,*R*,*S*)-**2** (0.50 g, 2.3 mmol), under argon atmosphere, in toluene (20 mL) and paraformaldehyde (0.41 g, 14 mmol) was heated to reflux for 1.5 h, cooled to rt, and concentrated under vacuum. The product was purified by column chromatography on deactivated silica gel [$Et_3N/SiO_2 = 2.5\%$ v/v, hexanes–EtOAc (95:5)].

4.4. (3a*S*,7a*S*)-3-*N*-[(*S*)-α-Phenylethyl]-octahydrobenzo-[*d*]oxazole, (*S*,*S*,*S*)-4

0.50 g (96% yield) as white solid, mp = 80–82 °C; $[\alpha]_D = +39.8$ (*c* 1, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.79–0.84 (m, 2H), 0.90–1.31 (m, 3H), 1.34 (d, 3H, $J = 6.6$ Hz), 1.43 (dd, 1H, $J = 3.0$ Hz, $J' = 11.4$ Hz), 1.63–1.72 (m, 1H), 1.91–2.08 (m, 2H), 3.32–3.39 (m, 1H), 3.48 (q, 1H, $J = 6.6$ Hz), 4.26 (d, 1H, $J = 2.6$ Hz), 4.80 (d, 1H, $J = 2.6$ Hz), 7.22–7.36 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 23.1, 24.4, 25.1, 30.7, 30.9, 63.7, 68.8, 83.4, 85.8, 127.0, 127.3, 127.9, 144.5; Colorless plate, $0.7 \times 0.7 \times 0.3$ mm^3, $C_{15}H_{21}NO$. Monoclinic, $P2_1$, $a = 5.5837(5)$, $b = 11.6568(13)$, $c = 10.3392(8)$ Å, $\beta = 97.912(5)°$, $Z = 2$, $\rho_{calc} = 1.153$ g cm^{-3}. A set of 7043 reflections was collected at $T = 296(1)$ K using Mo-K_α radiation ($\lambda = 0.71073$ Å, Bruker P4 diffractometer), corresponding to $2\theta_{max} = 60°$. 2034 independent reflections ($R_{int} = 0.0359$) were used for the refinement of 156 parameters, without neither restraints nor constraints (SHELXTL 5.10 package).[22] All H atoms were placed in idealized positions and refined using a standard riding model. The absolute configuration was assigned as (*S*,*S*,*S*) assuming the same configuration as for the starting material (*S*,*S*,*S*)-**1a**. Final *R* indices: $R_1 = 0.0371$ for 1858 reflections with $I > 2\sigma(I)$ and $wR_2 = 0.1123$ for all data. CCDC deposition number: 601707. Structure factors and raw files are available on request to authors. HRMS-FAB *m*/*z* found 232.1699 [$(M+H)^+$ calcd 232.1701 for $C_{15}H_{22}ON$].

4.5. (3a*R*,7a*R*)-3-*N*-[(*S*)-α-Phenylethyl]-octahydrobenzo-[*d*]oxazole, (*R*,*R*,*S*)-5

0.49 g (93% yield) as white solid, mp 96–97 °C; $[\alpha]_D = +23.8$ (*c* 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88–0.97 (m, 1H), 1.21–1.29 (m, 2H), 1.37 (d, 3H, $J = 6.6$ Hz), 1.48–1.52 (m, 1H), 1.68–1.78 (m, 2H), 2.06–2.18 (m, 3H), 3.34–3.38 (m, 1H), 3.73 (q, 1H, $J = 6.6$ Hz), 4.12 (d, 1H, $J = 3.6$ Hz), 4.40 (d, 1H, $J = 3.6$), 7.17–7.28 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.8, 24.5, 25.2, 30.7, 32.0, 63.6, 67.7, 83.2, 85.7, 126.6, 126.8, 127.9, 144.0; HRMS-FAB *m*/*z* found 232.1710 [$(M+H)^+$ calcd 232.1701 for $C_{15}H_{22}ON$].

4.6. (4a*S*,8a*S*)- and (4a*R*,8a*R*)-4-*N*-[(*S*)-α-Phenylethyl]-octahydrobenzo[1,4]oxazin-2-one, (*S*,*S*,*S*)-6 and (*R*,*R*,*S*)-7

These 4-oxazin-2-ones were prepared from glyoxal (40% aqueous solution v/v) and β-aminoalcohols (*S*,*S*,*S*)-**1a** or (*R*,*R*,*S*)-**2,** according to the literature procedure.[15]

4.7. (3a*S*,7a*S*)- and (3a*R*,7a*R*)-3-*N*-[(*S*)-α-Phenylethyl]-hexahydrobenzoxazolidin-2-ones, (*S*,*S*,*S*)-8 and (*R*,*R*,*S*)-9

These oxazolidin-2-ones were prepared from methyl chloroformate and β-aminoalcohols (*S*,*S*,*S*)-**1a** or (*R*,*R*,*S*)-**2**, according to the literature procedure.[16]

4.8. (1*S*,2*S*)-*N*,*N*′-Di-[(*S*)-α-phenylethyl]cyclohexane-1,2-diamine, (*S*,*S*,*S*,*S*)-10

This (*S*,*S*,*S*,*S*)-1,2-diamine was prepared from the *N*-[(*S*)-α-phenylethyl]cyclohexene aziridine and (*S*)-α-phenylethylamine as described in the literature.[17]

4.9. (1*S*,2*S*)-*N*-[(*S*)-α-Phenylethyl]-cyclohexane-1,2-diamine (*S*,*S*,*S*)-11

To a solution of 2-azido-amine (*S*,*S*,*S*)-**20** (0.29 g, 1.2 mmol) in methanol (10 mL) was added $Pd(OH)_2/C$ 10% mol (0.11 g). The mixture was stirred for 24 h at rt under H_2 atmosphere (1 atm). The crude product was filtered over Celite and washed with EtOAc (30 mL). The combined organic extract was evaporated and purified by column chromatography on silica gel [hexanes–EtOAc (1:2)]. The product was recovered as a colorless oil (0.25 g, 96% yield); $[\alpha]_D = +28.5$ (*c* 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.78–0.90 (m, 1H), 1.13–1.24 (m, 3H), 1.33 (d, 3H, $J = 6.4$ Hz), 1.58–1.65 (m, 2H), 1.88–1.93 (m, 2H), 2.16–2.21 (m, 1H), 2.31–2.36 (m, 1H), 2.6 (br, 3H), 3.88 (q, 1H, $J = 6.4$ Hz), 7.18–7.35 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.6, 25.0, 25.5, 32.4, 34.6, 55.7, 55.8, 61.3, 126.3, 126.6, 128.1, 146.8; HRMS-FAB *m*/*z* found 219.1867 $(M+H)^+$ calcd 219.1861 for $C_{14}H_{23}N_2$.

4.10. *tert*-Butyl (1*S*,2*S*)-2-*N*-[(*S*)-α-phenylethylamino]cyclohexylcarbamate, (*S*,*S*,*S*)-12

A solution of diamine (*S*,*S*,*S*)-**11** (0.20 g, 0.91 mmol), di-*tert*-butyl dicarbonate (0.22 mL, 1.0 mmol), and K_2CO_3 (0.12 g, 0.91 mmol) in $CHCl_3$ (25 mL) was stirred for 24 h. The mixture was extracted with CH_2Cl_2 (3×15 mL). The combined organic layer was dried with Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel [hexane–EtOAc (4:1)]. The product was recovered as a white solid (0.28 g, 98% yield); mp 79–80 °C; $[\alpha]_D = -17.5$ (*c* 1, $CHCl_3$); ^{1}H NMR ($CDCl_3$/TMS) δ 1.05–1.24 (m, 4H), 1.28 (d, 3H, $J = 6.6$ Hz), 1.47 (s, 9H), 1.54–1.61 (m, 3H), 1.74–1.80 (m, 1H), 2.00–2.05 (m, 1H), 2.15–2.25 (m, 1H), 3.22–3.27 (m, 1H), 3.90 (q, 1H, $J = 6.6$ Hz), 4.53 (d, 1H, $J = 7.0$ Hz), 7.15–7.35 (m, 5H); ^{13}C NMR ($CDCl_3$/TMS) δ 25.5, 29.2, 33.6, 34.2, 55.9, 57.3, 60.5, 79.4, 126.4, 128.0, 146.5, 155.6; HRMS-FAB *m*/*z* found 319.2378 $[(M+H)^+$ calcd 319.2386 for $C_{19}H_{31}N_2O_2$].

4.11. (3a*S*,7a*S*)-1,3-*N*,*N*′-Bis-[(*S*)-α-phenylethyl]-octahydro-1*H*-benzo-[*d*]-imidazole (*S*,*S*,*S*,*S*)-13

Diamine (*S*,*S*,*S*,*S*)-**10** (1.8 g, 5.6 mmol) was added to a mixture of 37% aqueous solution of formaldehyde (0.30 mL, 11 mmol), K_2CO_3 (2.0 g, 15 mmol), and $MgSO_4$ (2.0 g, 17 mmol) in $CHCl_3$ (25 mL) under argon atmosphere. The reaction mixture was stirred at rt for 24 h. The mixture was extracted with CH_2Cl_2 (3×15 mL). The combined organic layer was dried with Na_2SO_4, filtered and evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel [hexane–EtOAc (10:1)]. The product was obtained as a colorless liquid (1.8 g, 98% yield); $[\alpha]_D = +15.8$ (*c* 1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87–1.00 (m, 8H), 1.36 (d, 6H, $J = 6.6$ Hz), 2.25–2.34 (m, 2H), 3.60 (q, 2H, $J = 6.6$ Hz), 3.77 (s, 2H), 7.28–7.42 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.6, 24.5, 31.0, 61.6, 68.7, 71.2, 126.9, 127.7, 128.1, 145.2; HRMS-FAB *m*/*z* found 335.2477 $[(M+H)^+$ calcd 335.2487 for $C_{23}H_{31}N_2$].

4.12. (3a*S*,7a*S*)-*tert*-Butyl-3-*N*-[(*S*)-α-phenylethyl]-octahydrobenzo[*d*]imidazole-1-carboxylate, (*S*,*S*,*S*)-14

The diamine (*S*,*S*,*S*)-**11** (1.8 g, 8.3 mmol), was added to formaldehyde (37% aqueous solution) (0.45 mL, 17 mmol), K_2CO_3 (2.9 g, 21 mmol), and $MgSO_4$ (3.0 g, 25 mmol) in CH_2Cl_2 (25 mL) under inert atmosphere and stirred at rt for 4 h. Di-*tert*-butyl carbonate, $(Boc)_2O$ (2.1 mL, 9.1 mmol) was then added and the resulting solution was stirred for a further 24 h. The reaction mixture was extracted with CH_2Cl_2 (3×20 mL). The combined organic layer was dried with Na_2SO_4, filtered, and evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel [hexane–EtOAc (4:1)]. The product was isolated as white crystals, mp 75–76 °C (2.7 g, 98% yield); $[\alpha]_D = +96.1$ (*c* 1, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.78–0.94 (m, 1H), 1.06–1.26 (m, 4H), 1.33 (d, 3H, $J = 6.6$ Hz), 1.45 (s, 9H), 1.52–1.66 (m, 2H), 2.09 (dt, 1H, $J = 2.8$ Hz, $J' = 10.6$ Hz), 2.48 (br, 1H), 3.02–3.12 (m, 1H), 3.46 (q, 1H, $J = 6.6$ Hz), 3.66 (d, 1H, $J = 6.0$ Hz), 4.55 (br, 1H), 7.19–7.35 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 22.0, 24.9, 25.3, 29.2, 30.7, 31.0, 61.9, 63.5, 67.9, 71.1, 79.7, 126.7, 126.8, 127.9, 144.8, 154.2; HRMS-FAB *m*/*z* found 331.2381 $[(M+H)^+$ calcd 331.2386 for $C_{20}H_{31}O_2N_2$].

4.13. (4a*S*,8a*S*)-1,4-*N*,*N*′-Bis[(*S*)-α-phenylethyl]-octahydroquinoxalin-2(1*H*)-one, (*S*,*S*,*S*,*S*)-15

Diamine (*S*,*S*,*S*,*S*)-**10** (0.50 g, 1.5 mmol), in CH_2Cl_2 (10 mL), was added to glyoxal (1.5 mmol, 2.5 mL, 40% aqueous solution v/v) at rt and the solution was stirred for 24 h. The mixture was extracted with CH_2Cl_2 (3×20 mL) and the combined organic layer was dried with K_2CO_3, filtered, and evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel [hexane–EtOAc (6:1)]. The product was a yellow liquid (0.53 g, 98% yield); $[\alpha]_D = +5.0$ (*c* 1, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.82–0.94 (m, 1H), 1.10–1.17 (m, 3H), 1.24 (d, 3H, $J = 6.6$ Hz), 1.51–1.58 (m, 2H), 1.64 (d, 3H, $J = 7.3$ Hz), 1.90–1.97 (m, 1H), 2.12–2.17 (m, 1H), 2.40–2.48 (m, 1H), 2.97–3.07 (m, 1H), 3.13 (s, 2H), 4.27 (q, 1H, $J = 7.0$ Hz), 5.48 (q, 1H, $J = 7.0$ Hz), 7.15–7.41 (m, 10H); ^{13}C RMN (50 MHz, $CDCl_3$) δ 9.7, 19.4, 24.9, 25.4, 29.1, 31.3, 50.9, 52.8, 53.3, 62.4, 62.7, 126.2, 126.3, 126.8, 127.4, 127.7, 139.5, 142.1, 168.4; HRMS-FAB *m*/*z* found 363.2444 $[(M+H)^+$ calcd 363.2436 for $C_{24}H_{31}O_1N_2$].

4.14. (1*S*,2*S*)-*N*,*N*′-Bis-[(*S*)-α-phenylethyl]-*N*,*N*′-bis-(methylacetate)-1,2-cyclohexanediamine, (*S*,*S*,*S*,*S*)-16

A solution of 1,2-diamine (*S*,*S*,*S*,*S*)-**10** (3.5 g, 11 mmol), in acetonitrile (50 mL) and dry Na_2CO_3 (2.8 g, 26 mmol) was

treated under argon atmosphere with ethyl bromoacetate (4.1 g, 26 mmol). The resulting mixture was heated to reflux for 15 h, and cooled to rt. The organic solution was washed with 25 mL of H_2O, extracted with 3×25 mL of CH_2Cl_2, and the combined organic phase was dried over $MgSO_4$. The solvent was then removed under reduced pressure and the product was purified by column chromatography on silica gel [hexanes–EtOAc (10:1)]. The product was recovered as a colorless oil (4.0 g, 78% yield); $[\alpha]_D = +20.5$ (c 1, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.09–1.12 (m, 4H), 1.30 (d, 6H, $J = 7.0$ Hz), 1.61–1.70 (m, 2H), 2.09 (br, 2H), 2.93–2.97 (m, 2H), 3.18 (d, 2H, $J = 17.6$ Hz), 3.59 (s, 6H), 3.63 (d, 2H, $J = 16.6$ Hz), 4.55 (q, 2H, $J = 7.0$ Hz), 7.17–7.31 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.6, 26.8, 30.1, 47.7, 51.6, 57.5, 59.1, 126.3, 127.3, 127.9, 145.6, 173.7; HRMS-FAB m/z found 467.2905 [$(M+H)^+$ 467.2910 for $C_{28}H_{39}N_2O_4$].

4.15. (1*S*,2*S*)-*N*,*N*′-Bis[(*S*)-α-phenylethyl]-bis(2-hydroxyethyl)-1,2-cyclohexanediamine, (*S*,*S*,*S*,*S*)-17

A suspension of (*S*,*S*,*S*,*S*)-**16** (0.12 g, 0.26 mmol) and $LiAlH_4$ (0.051 g, 1.4 mmol) in THF (50 mL) was stirred under argon atmosphere for 24 h at rt. An aqueous saturated solution of NH_4Cl (10 mL) was added to quench the reaction. The organic solution was extracted with 3×25 mL of CH_2Cl_2 and the combined organic phase was dried over $MgSO_4$. The solvent was then removed under reduced pressure and the product was purified by column chromatography on silica gel [hexanes–EtOAc (10:1)]. The product was recovered as colorless crystals, mp = 183–184 °C (0.085 g, 80% yield), $[\alpha]_D = +47.0$ (c 1, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.12–1.21 (m, 4H), 1.39 (d, 6H, $J = 7$ Hz), 1.75–1.82 (m, 2H), 1.96–2.02 (m, 2H), 2.51–2.69 (m, 2H), 2.88–3.08 (m, 8H), 3.82 (br, 2H), 5.11 (br, 2H), 7.09–7.37 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.5, 25.4, 26.6, 50.2, 60.7, 62.3, 126.9, 127.8, 128.1, 144.6; HRMS-FAB+ m/z found 411.3003 [$(M+H)^+$ calcd 411.3012 for $C_{26}H_{39}N_2O_2$].

4.16. (1*S*,2*S*)-*N*,*N*′-Bis[(*S*)-α-phenylethyl]-bis[(*R*)-2-hydroxyphenethyl]-1,2-cyclohexanediamine, (*S*,*S*,*S*,*S*,*R*,*R*)-18

A solution of 1,2-diamine (*S*,*S*,*S*,*S*)-**10** (1.9 g, 5.8 mmol), in acetonitrile (20 mL) and lithium perchlorate (1.2 g, 12 mmol) was stirred under argon atmosphere until complete dissolution before the addition of (*R*)-styrene oxide (1.3 mL, 12 mmol). The resulting mixture was refluxed for 32 h, and cooled to rt. The organic solution was washed with 25 mL of H_2O, extracted with 3×25 mL of CH_2Cl_2, and the combined organic phase was dried over $MgSO_4$. The solvent was then removed under reduced pressure and the product was purified by column chromatography on silica gel [hexane–EtOAc (10:1)]. The product was recovered as a yellowish oil (2.4 g, 75% yield); $[\alpha]_D = -0.70$ (c 1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.58–0.72 (m, 1H), 0.84–0.95 (m, 1H), 1.04–1.17 (m, 2H), 1.22 (d, 3H, $J = 6.6$ Hz), 1.31–1.34 (m, 1H), 1.37 (d, 3H, $J = 6.9$ Hz), 1.47–1.57 (m, 2H), 1.71–1.80 (m, 4H), 2.25–2.28 (m, 1H), 2.66–2.78 (m, 3H), 3.18 (dd, 1H, $J = 3.0$ Hz, $J = 14.4$ Hz), 3.73 (dd, 1H, $J = 6.6$ Hz, $J' = 12.0$ Hz), 3.83 (q, 1H, $J = 6.6$ Hz), 4.01 (q, 1H, $J = 7.2$ Hz,), 4.46 (br, 1H), 7.18–7.37 (m, 20H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.3, 23.7, 23.9, 25.0, 26.1, 29.0, 32.6, 32.7, 55.7, 56.1, 56.2, 59.2, 60.3, 75.5, 125.9, 126.6, 126.7, 126.8, 127.0, 127.5, 128.2, 128.3, 143.3, 145.2, 147.5, 147.6; HRMS-FAB+ m/z found 563.3636 [$(M+H)^+$ calcd 563.3638 for $C_{38}H_{47}N_2O_2$].

4.17. *N*-[(*S*)-α-Phenylethyl]cyclohexene aziridine, (*S*)-19

The aziridine was prepared from the diastereoisomeric mixture of β-aminoalcohols (*S*,*S*,*S*)-**1a** and (*R*,*R*,*S*)-**2**, according to the literature procedure.[16]

4.18. (1*S*,2*S*)-2-Azido-*N*-[(*S*)-α-phenylethyl]cyclohexanamine, (*S*,*S*,*S*)-20

In a dry two-necked flask fitted with condenser and magnetic stirrer were placed aziridine (*S*)-**19** (6.0 g, 30 mmol) and $CeCl_3{\cdot}7H_2O$ (5.5 g, 15 mmol) in a mixture of CH_3CN–H_2O (9:1, 30 mL). To the stirred solution was added NaN_3 (2.1 g, 33 mmol) at rt and the reaction mixture was heated to reflux for 8 h. The organic phase was extracted with CH_2Cl_2 (3×25 mL) and H_2O (25 mL). The combined organic layer was dried with Na_2SO_4, and evaporated under reduced pressure. The separation of the major diastereomeric *trans*-2-azido amine was performed by column chromatography on deactivated silica gel [Et_3N/SiO_2 = 2.5% v/v, hexanes–EtOAc (30:1)], (*S*,*S*,*S*)-**20** was recovered as a colorless liquid (4.2 g, 58% yield); $[\alpha]_D = +23.5$ (c 1, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.10–1.27 (m, 4H), 1.33 (d, 3H, $J = 6.6$ Hz), 1.44 (s, 1H), 1.49–1.60 (m, 1H), 1.64–1.75 (m, 2H), 1.92–2.11 (m, 1H), 2.29–2.40 (m, 1H), 3.04–3.21 (m, 1H), 3.89 (q, 1H, $J = 6.6$ Hz), 7.16–7.39 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 24.3, 24.4, 30.6, 32.5, 56.6, 59.4, 66.3, 126.5, 126.7, 128.3, 147.2; HRMS-FAB+ m/z found 245.1756 [$(M+H)^+$ calcd 245.1766 for $C_{14}H_{21}N_4$].

4.19. *N*,*N*′-Bis[(*S*)-α-phenylethyl]-1,2-ethylenediamine, (*S*,*S*)-21

The diamine was prepared from 1,2-dichloroethane and (*S*)-α-phenylethylamine, according to the literature procedure.[19]

4.20. *N*,*N*′-Bis[(*S*)-α-phenylethyl]-bis[(*R*)-hydroxyphenethyl]-1,2-ethylenediamine, (*S*,*S*,*R*,*R*)-22

A solution of 1,2-diamine (*S*,*S*)-**21** (2.7 g, 10 mmol) in acetonitrile (20 mL) and lithium perchlorate (2.1 g, 20 mmol) was stirred under argon atmosphere until complete dissolution. (*R*)-Styrene oxide (2.4 g, 20 mmol) was added to the reaction mixture and the resulting mixture was heated to reflux for 36 h, and cooled to rt. The organic solution was washed with 25 mL of H_2O, extracted with 3×25 mL of CH_2Cl_2, and the combined organic phase was dried over $MgSO_4$. The solvent was then removed under reduced pressure and the product was purified by column chromatography on silica gel [hexanes–EtOAc (8:1)] affording a colorless liquid (3.5 g, 70% yield); $[\alpha]_D = -47.2$ (c 1.10, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ

1.49 (d, 6H, $J = 6.6$ Hz), 2.38–2.70 (m, 6H), 2.84–2.89 (m, 2H), 3.98 (q, 2H, $J = 6.6$ Hz), 4.58–4.63 (m, 2H), 4.80 (br, 2H), 7.21–7.28 (m, 20H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.4, 49.5, 59,7, 60.1, 70.7, 125.8, 127.3, 127.4, 128.2, 128.3, 140.9, 142.3. The diamine dihydrochloride was prepared adding HCl 10% ethereal solution (10 mL), affording white crystals, mp 165–166 °C. Elemental analysis: found C 68.34%, H 7.75% [calcd for $C_{34}H_{40}N_2O_2{\cdot}2HCl{\cdot}H_2O$: C 68.09%, H 7.39%].

4.21. Diethylzinc addition to benzaldehyde

The ligands **4**–**18** and **22** (6 mol %) were weighed into the reaction vessel and diethylzinc (1.0 M toluene, 2.03 equiv, 0.94 mL) was added at rt. After 10 min, benzaldehyde (1.0 equiv, 0.47 mmol) was added neat. The homogeneous reaction mixture was stirred at rt. After 20 h the reaction was quenched with water (5 mL), diluted with EtOAc, filtered through Celite, and the layers separated. The aqueous layer was extracted with EtOAc (2×40 mL) and the combined organic layers washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography on deactivated silica gel [$Et_3N/SiO_2 = 2.5\%$ v/v, hexanes–EtOAc (97:3)] to afford 1-phenyl-1-propanol **3**.[11]

Acknowledgments

This work was supported by CONACYT, Consejo Nacional de Ciencia y Tecnología (Project V39500-Q and Scholarships No. 144893, 144937, and 145001).

References

1. Mukaiyama, T.; Soai, K.; Sato, T.; Shimizu, H.; Suzuki, K.. *J. Am. Chem. Soc.* **1979**, *101*, 1455–1460.
2. Oguni, N.; Omi, T. *Tetrahedron Lett.* **1984**, *25*, 2823–2824.
3. Noyori, R.; Kitamura, M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 49–69.
4. Soai, K.; Niwa, S. *Chem. Rev.* **1992**, *92*, 833–856.
5. Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; Wiley: New York, 1994.
6. Soai, K.; Shibata, T. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Berlin, 1999; pp 911–922.
7. Pu, L.; Yu, H.-B. *Chem. Rev.* **2001**, *101*, 757–824.
8. Juaristi, E.; Escalante, J.; León-Romo, J. L.; Reyes, A. *Tetrahedron: Asymmetry* **1998**, *9*, 715–740.
9. Juaristi, E.; León-Romo, J. L.; Reyes, A. *Tetrahedron: Asymmetry* **1999**, *10*, 2441–2495.
10. (a) Anaya de Parrodi, C.; Juaristi, E.; Quintero-Cortés, L. *An. Quím., Int. Ed.* **1996**, *92*, 400–404; (b) Anaya de Parrodi, C.; Juaristi, E.; Quintero-Cortés, L.; Amador, P. *Tetrahedron: Asymmetry* **1996**, *7*, 1915–1918.
11. Sosa-Rivadeneyra, M.; Muñoz-Muñiz, O.; Anaya de Parrodi, C.; Quintero, L.; Juaristi, E. *J. Org. Chem.* **2003**, *68*, 2369–2375.
12. (a) Cobb, A. J. A.; Marson, C. M. *Tetrahedron* **2005**, *61*, 1269–1279; (b) Trost, B. M.; Crawley, M. L. *Chem. Rev.* **2003**, *103*, 2921–2943.
13. (a) Prasad, K. R. K.; Joshi, N. N. *J. Org. Chem.* **1997**, *62*, 3770–3771; (b) Braga, A. L.; Appelt, H. R.; Schneider, P. H.; Silveira, C. C.; Wessjohann, L. A. *Tetrahedron: Asymmetry* **1999**, *10*, 1733–1738; (c) Abato, P.; Seto, C. T. *J. Am. Chem. Soc.* **2001**, *123*, 9206–9207.
14. Okaniwa, M.; Yanada, R.; Ibuka, T. *Tetrahedron Lett.* **2000**, *41*, 1047–1050.
15. Sosa-Rivadeneyra, M.; Quintero-Cortés, L.; Anaya de Parrodi, C.; Bernès, S.; Castellanos, E.; Juaristi, E. *Arkivoc* **2003**, *Part (xi)*, 61–71.
16. Anaya de Parrodi, C.; Juaristi, E.; Quintero, L.; Clara-Sosa, A. *Tetrahedron: Asymmetry* **1997**, *8*, 1075–1082.
17. (a) Anaya de Parrodi, C.; Moreno, G. E.; Quintero, L.; Juaristi, E. *Tetrahedron: Asymmetry* **1998**, *9*, 2093–2099; (b) Anaya de Parrodi, C.; Vázquez, V.; Quintero, L.; Juaristi, J. *Synth. Commun.* **2001**, *31*, 3295–3302.
18. Cf. Chandrasekhar, M.; Sekar, G.; Singh, V. K. *Tetrahedron Lett.* **2000**, *41*, 10079–10083.
19. (a) Hulst, R.; deVries, K. N.; Feringa, B. L. *Tetrahedron: Asymmetry* **1994**, *5*, 699–708; (b) Mimoun, H.; de Saint Laumer, J. Y.; Giannini, L.; Scopelliti, R.; Floriani, C. *J. Am. Chem. Soc.* **1999**, *121*, 6158–6166; (c) Mastranzo, V. M.; Quintero, L.; Anaya de Parrodi, C.; Juaristi, E.; Walsh, P. J. *Tetrahedron* **2004**, *60*, 1781–1789.
20. (a) Niwa, S.; Soai, K. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2717–2720; (b) Pini, D.; Mastantuono, A.; Ucello-Barreta, G.; Iuliano, A.; Salvadori, P. *Tetrahedron* **1993**, *49*, 9613–9624; (c) Eilers, J.; Wilken, J.; Martens, J. *Tetrahedron: Asymmetry* **1996**, *7*, 2343–2357; (d) Asami, M.; Inoue, S. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 1687–1690; (e) Brunel, J.-M.; Constantieux, T.; Legrand, O.; Buono, G. *Tetrahedron Lett.* **1998**, *39*, 2961–2964; (f) Saravanan, P.; Bisai, A.; Baktharaman, S.; Chandrasekhar, M.; Singh, V. K. *Tetrahedron* **2002**, *58*, 4693–4706.
21. Masamune, S.; Choy, W.; Petersen, J. S.; Sita, L. R. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1–30.
22. Sheldrick, G. M. SHELXTL-*Plus Release 5.10*; Bruker AXS: Madison, WI, USA, 1998.