Novel preparation of non-racemic 1-[α-(1-azacycloalkyl)benzyl]-2-naphthols from Betti base and their application as chiral ligands in the asymmetric addition of diethylzinc to aryl aldehydes

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A novel route for the preparation of non-racemic 1-[α-(1-azacycloalkyl)benzyl]-2-naphthols was developed, which involves regioselective *N*-cycloalkylation of the Betti base with dials in the presence of $NaBH_3CN$ to give 1-azacycloalka[2,1-*b*]oxazine followed by the selective cleavage of a C–O bond with $LiAlH_4$. As a new family of chiral ligands, their application in the enantioselective addition of diethylzinc to aryl aldehydes was tested. The ligands incorporating pyrrolidine and piperidine led to highly efficient asymmetric induction to give products in up to 96% yield and 99% ee.

Introduction

Chiral ligands with 1,2- and 1,3-amino-hydroxy structures have been employed widely in a variety of asymmetric syntheses catalyzed by metallic ions and most of them were derived from a few readily available natural products.[1] To increase the understanding of asymmetric reactions, the design and synthesis of chiral ligands from non-natural resources are essential.[2] Therefore, chiral amino-phenol compounds have recently been gaining in importance.[3]

1-(α-Aminobenzyl)-2-naphthol (**1**, Betti base) has the desired 1,3-amino-hydroxy structure and its racemic compound is available in bulk.[4] Although its enantiomers, (*S*)-**1** and (*R*)-**1**, were reported early last century (Chart 1),[5] they were never

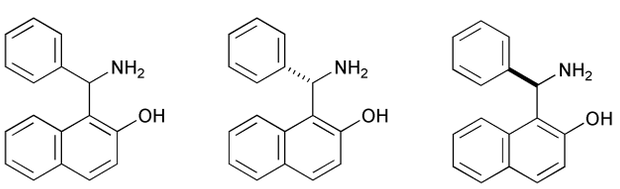

Chart 1

employed as chiral ligands in asymmetric synthesis until the work of Cardellicchio *et al.* in 1998,[3b,c] in which the resolution procedure was modified and the *N*,*N*-dimethyl derivative of (*S*)-**1** induced the asymmetric addition of diethylzinc to aryl aldehydes in up to 99% ee. Since then, several other non-racemic *N*,*N*-dialkylated derivatives of the chiral Betti base have been reported to give excellent asymmetric inductions.[3e–g]

Non-racemic amine derivatives of the Betti base showed very similar behavior to other reported amino-hydroxy ligands. Its tertiary amines gave better results than primary and secondary amines in most cases.[3c,f] However the non-racemic *N*,*N*-dialkylated derivatives of the Betti base that have been reported in the literature were usually prepared by resolution of the corresponding racemic isomers[3b,c,5] or by condensation with chiral amines[3e–g] rather than directly from *N*,*N*-dialkylation of (*S*)-**1** or (*R*)-**1**. This result strongly implies that there is no suitable method for the regioselective *N*,*N*-dialkylation of the Betti base so far and that the uses of the non-racemic Betti base, (*S*)-**1** or (*R*)-**1**, as a new chiral resource are seriously limited.

Herein, we would like to report a novel synthetic route by which to prepare a new family of chiral cyclic amino-phenol ligands **4a**–**f** by direct *N*-cycloalkylation of (*S*)-**1** and (*R*)-**1**. In the enantioselective addition of diethylzinc to aryl aldehydes, these ligands gave highly efficient asymmetric induction to give products in up to 96% yield and 99% ee.

Results and discussion

Very recently, several attractive procedures were reported for the regioselective *N*-cycloalkylation of amino-hydroxy compounds. For example, 1,2-aliphatic amino-alcohols can be *N*-cycloalkylated using dihalides and a variety of bases,[6] and *N*-cycloalkylation of 1,3-aromatic amino-phenol has been achieved by reductive amination with dial in the presence of $NaBH_4$ and H_2SO_4.[3a] Unfortunately, all of our initial attempts at regioselective *N*-cycloalkylation of (*S*)-**1** using these procedures failed. Thus, a mixture of *O*-alkylated products was obtained when (*S*)-**1** was treated with 1,5-dibromopentane and bases, and pentane-1,5-diol was produced almost quantitatively in the reductive amination of (*S*)-**1** with pentane-1,5-dial and $NaBH_4$–H_2SO_4. These results may explain why the Betti base is a 1,3-aliphatic amino-phenol compound and that the reactions lack selectivity due to the relatively low reactivity of the aliphatic amine and the higher reactivity of the phenol.

However, the reaction of 1,2-amino-alcohols with pentane-1,5-dial to yield 1-azacycloalka[2,1-*b*]oxazoles has attracted our interest. The reactions usually proceed in the presence of a nucleophilic reagent, such as benzotriazole[7] or CN^-[8] to yield substituted 1-azacycloalka[2,1-*b*]oxazole derivatives (**2**) (Scheme 1). The mechanism suggests that an unsubstituted 1-azacycloalka[2,1-*b*]oxazine (**3b**) could be obtained by replacement of 1,2-amino-alcohols with the Betti base and by using H^- as a nucleophilic species.

As expected, when (*S*)-**1** was treated with pentane-1,5-dial in the presence of $NaBH_3CN$ in an aqueous buffer solution[9] (Na_2HPO_4–KH_2PO_4), unsubstituted tetrahydropyrido-[2,1-*b*]oxazine **3b** was obtained in 76% yield over 12 days (monitored by TLC) (Scheme 2). Fortunately, the reaction time

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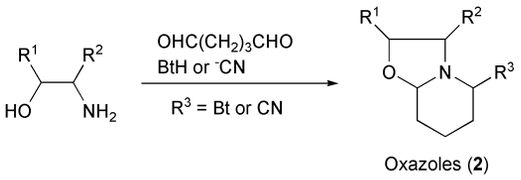
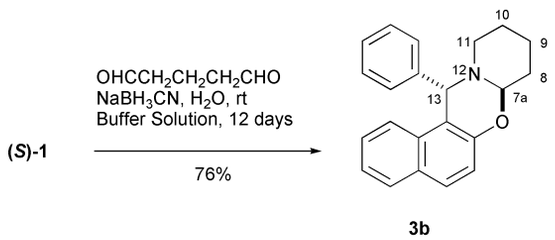
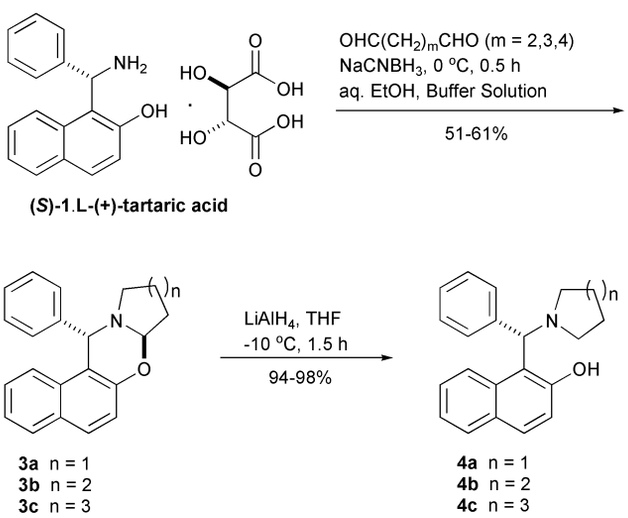


Scheme 1



Scheme 2

can be shortened considerably by increasing the ratio of EtOH in the reaction solvent. In practice, the salt of **(*S*)-1** with L-(+)-tartaric acid, which is a precursor of **(*S*)-1** in its optical resolution, was used directly as the starting material and **3b** was obtained in 61% yield within 30 min in 50% aqueous EtOH (Scheme 3). The ^{1}H NMR signal due to the proton of the newly



Scheme 3

formed chiral carbon was readily assigned to the formation of an oxazine ring. As shown in Fig. 1, the structure of **3b** was confirmed and the relative stereochemistry of the newly formed chiral carbon was established as the *R*-configuration by single crystal X-ray diffraction analysis.[10] Similarly, **3a** (59%) and **3c** (51%) were prepared respectively by the replacement of pentane-1,5-dial with butane-1,4-dial and hexane-1,6-dial under the same conditions.

Normally, the selective cleavage of the C–O bond in oxazolo-[3,2-*a*]pyridines (**2**) can be effected by $NaBH_4$ at room temperature over several hours.[3b–d,7b] This procedure also works well for the selective cleavage of the C–O bond in the tetrahydropyrido[2,1-*b*]oxazine ring (**3b**) in satisfactory yield, but the optical purity of the product is reduced. Therefore, compound **3b** was treated with $LiAlH_4$ at −10 °C for 1.5 h and the desired amino-phenol **4b** was obtained in 94% yield without any loss of enantiomeric excess. Similarly, reductions of **3a** and **3c** gave **4a** and **4c**, respectively, in excellent yields (Scheme 3).

By exactly the same route as followed in the preparation of **3a**–**c** and **4a**–**c**, their *R*-counterparts **3d**–**f** and **4d**–**f** were prepared using the salt of **(*R*)-1** and D-(−)-tartaric acid as the starting material (Chart 2).

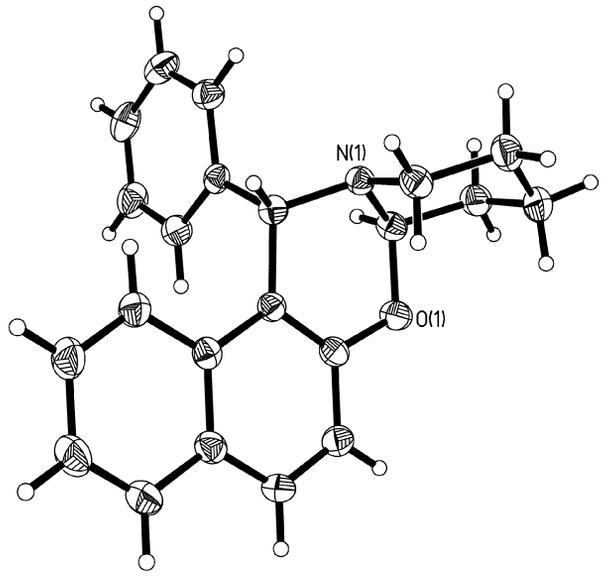
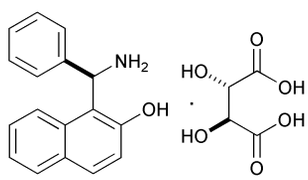


Fig. 1 X-Ray single crystal structure of compound **3b**.



(*R*)-1.D-(-)-tartaric acid

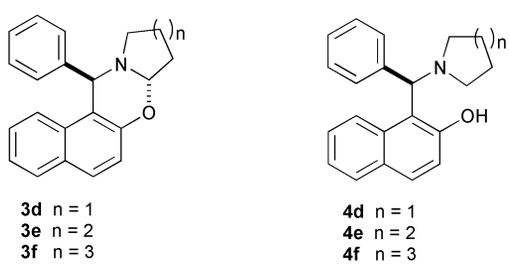


Chart 2

To determine the optical purities of **4a**–**f** by ^{1}H NMR, several chiral shift reagents were scanned to monitor the benzyl protons of **4a**–**f** and Eu(tfc) showed the best results. It was observed that the difference in the chemical shift between *R*- and *S*-benzyl protons increases with the size of the azacycloalkane, thus 0.0122 ppm (3.66 Hz) for pyrrolidine, 0.0493 ppm (14.79 Hz) for piperidine and 0.1033 ppm (30.98 Hz) for azepane. It was also observed that the chemical shifts of the hydroxy protons in **4a**–**f** are located at a very low-field, around δ 14.30–13.88 ppm, due to the presence of strong intramolecular hydrogen bonds between the hydroxy and amine groups (Fig. 2).

As shown in the X-ray single crystal structure of compound **4b** (Fig. 2),[10] its chiral carbon is attached to three rings to build a wonderful chiral molecular cave and a four-atom plane is defined by C1 and C2 on the naphthalene as well as the attached carbon and oxygen. Therefore, it is reasonable to expect that **4a**–**f**, as chiral ligands, could form conformationally rigid six-membered rings with metallic ions and that substrates could approach the center ions only from the side of the benzyl hydrogen.

The asymmetric addition of $ZnEt_2$ to benzaldehyde was tested initially in toluene with 5 mol% of **4b** to give 1-phenylpropanol as the product in 94% yield and 96% ee in 12 hours (Scheme 4). But using 10 mol% of **4b** produced better results (95% yield and 97% ee) in a shorter reaction time (8 h). It is

Table 1 Effect of temperature on the addition of $ZnEt_2$ to benzaldehydes with 10 mol% ligand **4b**

Entry	*T*/°C	*t*/h	Yield (%)[a]	Ee (%)[b]
1	−10	48	96	98
2	0	16	96	98
3	10	8	95	97
4	30	6	94	95
5	50	3	93	94

[a] Isolated yields. [b] Determined by chiral GC (10% permethylated β-CD).

Table 2 Enantioselective addition of $ZnEt_2$ to aryl aldehydes catalyzed by ligands **4a**–**f**

Entry	Ar	Ligands	Yield (%)[a]	Ee (%)[b]
1	C_6H_5-	**4a**	93	99 (*R*)
2	C_6H_5-	**4d**	91	98 (*S*)
3	C_6H_5-	**4b**	95	98 (*R*)
4	C_6H_5-	**4e**	91	98 (*S*)
5	4-$CH_3C_6H_4$-	**4b**	95	98 (*R*)
6	4-$CH_3OC_6H_4$-	**4b**	96	95 (*R*)
7	2-ClC_6H_4-	**4b**	95	91 (*R*)
8	4-FC_6H_4-	**4b**	96	98 (*R*)
9	4-$CF_3OC_6H_4$-	**4b**	94	95 (*R*)
10	C_6H_5-	**4c**	93	73 (*R*)
11	C_6H_5-	**4f**	92	75 (*S*)

[a] Isolated yields. [b] Determined by chiral GC (10% permethylated β-CD).

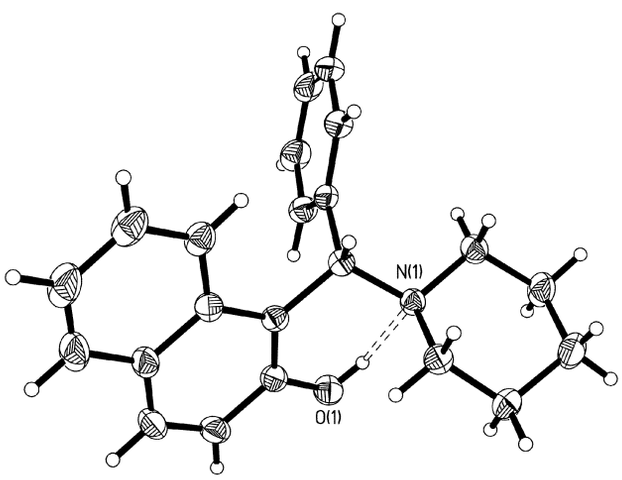
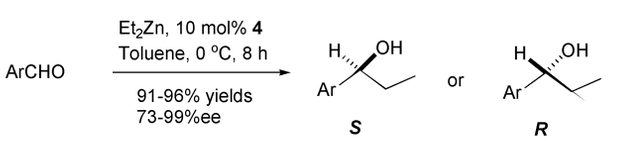


Fig. 2 X-Ray single crystal structure of compound **4b**.



Scheme 4

interesting to note that the enantioselectivity of the reaction is not very dependent on temperature (Table 1).

As illustrated in Table 2, the size of the azacycloalkane in ligands **4a**–**f** plays an important role in their induced asymmetric additions. Both pyrrolidine (**4a** and **4d**) and piperidine (**4b** and **4e**) gave products in excellent yields and enantiomeric excess (Entries 1–9), whilst azepane (**4c** and **4f**) gave products in moderate optical yields (Entries 10 and 11). It is worth mentioning that ligands **4a**–**f** can be recovered in 70–95% yields conveniently by filtration after the reaction and used repeatedly without any loss of reactivity.

In summary, a new family of chiral ligands (*S*)- and (*R*)-1-[α-(1-azacycloalkyl)benzyl]-2-naphthols (**4a**–**f**) have been prepared by selective *N*-cyclizations of (*S*)-(+)- and (*R*)-(−)-Betti bases with dials in the presence of $NaBH_3CN$ to give 1-azacycloalka[2,1-*b*]oxazines followed by selective cleavage of C–O bonds with $LiAlH_4$. The ligands with pyrrolidine and piperidine lead to highly efficient asymmetric induction in the addition of diethylzinc to aryl aldehydes with up to 96% yield and 99% ee.

Experimental

All melting points were determined on a Yanaco melting point apparatus and are uncorrected. IR spectra were recorded on a Nicolet FT-IR 5DX spectrometer as KBr pellets. The ^1H NMR spectra were recorded on a Bruker ACF-300 spectrometer in $CDCl_3$ with TMS as internal reference. The *J* values are given in Hz. MS spectra were obtained on a VG-ZAB-HS mass spectrometer at 70 eV. The elemental analyses were performed on a Perkin-Elmer 240C instrument. Optical rotations were determined on a Perkin-Elmer 241 polarimeter and are given in units of 10^{-1} deg cm² g^{-1}. The salts of (*S*)-**1**·L-(+)-tartaric acid (>99% ee) and (*R*)-**1**·D-(−)-tartaric acid (>99% ee) were prepared according to ref. 3*b*. PE is petroleum ether (60–90 °C).

General procedure for the preparation of 1-azacycloalka[2,1-*b*]-oxazines 3a–f

To a solution of (*S*)-**1** or (*R*)-**1** (as salts of tartaric acid, 6.4 g, 16 mmol) in 50% aqueous EtOH (600 mL) and buffer solution (1 : 1 Na_2HPO_4–KH_2PO_4, 1.0 M, 40 mL) was added $NaBH_3CN$ (1.3 g, 17 mmol) in one-portion and dial (25 mmol) dropwise at 0 °C. The mixture quickly became cloudy. After 30 min, the crude product, a white solid, was filtered off and was dissolved in EtOAc. The solution was washed with H_2O and brine, and dried over Na_2SO_4. The solvent was removed to yield the desired products.

(7a*R*,12*S*)-12-Phenyl-7a,8,9,10-tetrahydro-12*H*-naphtho[1,2-*e*]-pyrrolo[2,1-*b*][1,3]oxazine (3a)

Using (*S*)-**1**·L-(+)-tartaric acid and butane-1,4-dial,[7d] compound **3a** was obtained as white crystals in 59% yield; mp 97–98 °C (EtOAc–PE), $[\alpha]_D^{25}$ = +156.8 ($CHCl_3$, *c* 1.20) (Found: C, 83.67%; H, 6.60%; N, 4.75%. $C_{21}H_{19}NO$ requires: C, 83.69%; H, 6.35%; N, 4.65%); ν_{max}/cm^{-1} 3060, 2940, 2830, 1618, 1598; δ_H 7.80–7.73 (m, 2H), 7.43–7.40 (m, 8H), 7.33–7.27 (m, 1H), 5.48 (s, 1H), 5.12 (t, *J* 3.0, 1H), 3.40–3.33 (m, 1H), 2.95 (dd, *J* 8.4, 16.2, 1H), 2.14–1.97 (m, 4H); *m*/*z* 301 (M^+, 1.1%), 231 (100), 202 (31).

(7a*R*,13*S*)-13-Phenyl-8,9,10,11-tetrahydro-7a*H*,13*H*-naphtho-[1,2-*e*]pyrido[2,1-*b*][1,3]oxazine (3b)

Using (*S*)-**1**·L-(+)-tartaric acid and pentane-1,5-dial (25% aqueous solution), compound **3b** was obtained as white crystals in 61% yield; mp 179.5–181.5 °C (EtOAc–PE), $[\alpha]_D^{25}$ = +109 ($CHCl_3$, *c* 1.33) (Found: C, 83.61%; H, 6.52%; N, 4.50%. $C_{22}H_{21}NO$ requires: C, 83.78%; H, 6.71%; N, 4.44%); ν_{max}/cm^{-1} 3090, 2901, 2850, 1618, 1595; δ_H 7.75–7.72 (m, 2H), 7.45–7.16 (m, 9H), 5.21 (s, 1H), 4.94 (s, 1H), 2.92–2.88 (m, 2H), 2.03–1.98 (m, 1H), 1.85–1.71 (m, 3H), 1.67–1.59 (m, 2H); δ_C 152.7, 143.4, 133.2, 129.8 (2C), 129.5, 129.4, 129.0, 128.6 (2C), 127.6, 126.9, 123.4, 123.3, 119.2, 111.6, 81.8, 63.3, 48.8, 30.0, 25.9, 18.8; *m*/*z* 315 (M^+, 4.3%), 231 (100), 202 (23).

(7a*R*,14*S*)-14-Phenyl-7a,8,9,10,11,12-hexahydro-14*H*-naphtho-[1′,2′:5,6][1,3]oxazino[2,1-*b*]azepine (3c)

Using (*S*)-**1**·L-(+)-tartaric acid and hexane-1,6-dial,[11] compound **3c** was obtained as white crystals in 51% yield; mp 99–101 °C ($CHCl_3$–PE), $[\alpha]_D^{25}$ = +95.3 ($CHCl_3$, *c* 0.68) (Found: C, 83.70%; H, 7.32%; N, 4.00%. $C_{23}H_{23}NO$ requires: C, 83.85%; H, 7.04%; N, 4.25%); ν_{max}/cm^{-1} 3080, 3040, 2940, 2850, 1620, 1600; δ_H 7.81–7.74 (m, 2H), 7.38–7.28 (m, 8H), 7.10 (d, *J* 9.6, 1H), 5.30 (s, 1H), 4.89 (t, *J* 7.2, 1H), 3.27 (dd, *J* 9.5, 12.9, 1H),

2.73 (d, *J* 14.7, 1H), 2.24 (m, 1H), 1.92–1.72 (m, 5H), 1.53–1.28 (m, 2H); *m*/*z* 329 (M^+, 4.5%), 231 (100), 202 (30).

(7a*S*,12*R*)-12-Phenyl-7a,8,9,10-tetrahydro-12*H*-naphtho[1,2-*e*]-pyrrolo[2,1-*b*][1,3]oxazine (3d), (7a*S*,13*R*)-13-phenyl-8,9,10, 11-tetrahydro-7a*H*,13*H*-naphtho[1,2-*e*]pyrido[2,1-*b*][1,3]oxazine (3e) and (7a*S*,14*R*)-14-phenyl-7a,8,9,10,11,12-hexahydro-14*H*-naphtho[1′,2′:5,6][1,3]oxazino[2,1-*b*]azepine (3f)

By using (*R*)-**1**·D-(−)-tartaric acid with butane-1,4-dial, pentane-1,5-dial or hexane-1,6-dial, **3d**–**f** were produced respectively. Compounds **3d**–**f** had identical IR, ^{1}H NMR, MS and optical rotations (opposite direction) as their corresponding counterparts **3a**–**c**.

A general procedure for the preparation of 1-[α-(1-azacycloalkyl)-benzyl]-2-naphthols 4a–f

To a stirred solution of $LiAlH_4$ (570 mg, 15 mmol) in dry THF (20 mL) was added a solution of **3** (10 mmol) in THF (30 mL) dropwise at −10 °C. After stirring at this temperature for 1.5 h (monitored by TLC), it was quenched by the addition of a saturated aqueous solution of NH_4Cl (20 mL) and stirred for another 30 min. Then the mixture was extracted with CH_2Cl_2 (40 mL), and the organic layer was washed with brine and water, and dried over Na_2SO_4. The solvent was removed to give the desired products.

(*S*)-1-(α-Pyrrolidinylbenzyl)-2-naphthol (4a)

By reduction of **3a**, compound **4a** was obtained as white crystals in 93% yield; mp 159–161 °C (EtOAc), $[\alpha]_D^{25}$ = +179.1 ($CHCl_3$, *c* 1.30) (Found: C, 83.16%; H, 7.05%; N, 4.62%. $C_{21}H_{21}NO$ requires: C, 83.13%; H, 6.98%; N, 4.62%); ν_{max}/cm^{-1} 3120, 3080, 2970, 2840, 1452, 1200; δ_H 13.88 (s, 1H), 7.91 (d, *J* 8.6, 1H), 7.72–7.55 (m, 4H), 7.44–7.03 (m, 6H), 5.16 (s, 1H), 3.27 (br s, 1H), 2.44 (br s, 3H), 1.89 (br s, 4H); *m*/*z* 303 (M^+, 0.04%), 231 (100), 202 (30), 70 (13).

(*S*)-1-(α-Piperidylbenzyl)-2-naphthol (4b)

By reduction of **3b**, compound **4b** was obtained as white crystals in 94% yield; mp 194–196 °C (EtOAc–PE), $[\alpha]_D^{25}$ = +193.8 ($CHCl_3$, *c* 1.20) (Found: C, 83.16%; H, 7.25%; N, 4.36%. $C_{22}H_{23}NO$ requires: C, 83.24%; H, 7.30%; N, 4.41%); ν_{max}/cm^{-1} 3120, 1238; δ_H 14.01 (s, 1H), 7.86 (d, *J* 8.7, 1H), 7.72–7.57 (m, 4H), 7.38–7.16 (m, 6H), 5.10 (s, 1H), 3.35 (br s, 1H), 2.68 (br s, 1H), 2.15–1.70 (m, 8H); *m*/*z* 317 (M^+, 0.9%), 232 (48), 231 (100), 202 (23), 85 (11), 84 (43).

(*S*)-1-(α-Azepanylbenzyl)-2-naphthol (4c)

By reduction of **3c**, compound **4c** was obtained as white crystals in 95% yield; mp 117–117.5 °C (EtOAc–PE), $[\alpha]_D^{25}$ = +184.4 ($CHCl_3$, *c* 0.34) (Found: C, 83.41%; H, 7.56%; N, 4.18%. $C_{23}H_{25}NO$ requires: C, 83.34%; H, 7.60%; N, 4.23%); ν_{max}/cm^{-1} 3070, 2940, 2855, 1440, 1240; δ_H 14.30 (s, 1H), 7.90 (d, *J* 9.0, 1H), 7.71–7.62 (m, 4H), 7.39–7.36 (m, 1H), 7.29–7.14 (m, 5H), 5.32 (s, 1H), 2.73 (br m, 4H), 1.85–1.60 (m, 10H); *m*/*z* 331 (M^+, 0.2%), 231 (100), 203 (14), 202 (45), 201 (10), 200 (10), 99 (14).

(*R*)-1-(α-Pyrrolidinylbenzyl)-2-naphthol (4d), (*R*)-1-(α-piperidyl-benzyl)-2-naphthol (4e) and (*R*)-1-(α-azepanylbenzyl)-2-naphthol (4f)

By the reduction of **3d**–**f**, compounds **4d**–**f** were produced respectively. Compounds **4d**–**f** had identical IR, ^{1}H NMR, MS and optical rotations (opposite direction) as their corresponding counterparts **4a**–**c**.

General procedure for the addition of $ZnEt_2$ to aldehydes

To a stirred solution of **4** (0.5 mmol) and aldehyde (5 mmol) in dry toluene (10 mL) was added a solution of Et_2Zn in toluene (1.0 M, 11 mL, 11 mmol) by syringe at 0 °C under Ar. Eight hours later, a residue was obtained by regular work-up procedure. Then Et_2O (5 mL) was added and ligand **4** was precipitated in 70–95% yield as white crystals which were filtered off. The filtrate was concentrated and purified by chromatography to yield 1-phenylpropanols as shown in Scheme 4 and Table 2.

Acknowledgements

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References

1 For reviews, see: (*a*) K. Soai and S. Niwa, *Chem. Rev.*, 1992, **92**, 833; (*b*) D. J. Ager, I. Prakash and D. R. Schaad, *Chem. Rev.*, 1996, **96**, 835.
2 For selected recent reports, see: (*a*) A. Vidal-Ferran, A. Moyano, M. A. Pericas and A. Riera, *J. Org. Chem.*, 1997, **62**, 4970; (*b*) C. Bolm, K. Muniz-Fernandez, A. Seger, G. Raabe and K. Gunther, *J. Org. Chem.*, 1998, **63**, 7860; (*c*) K. S. Reddy, L. Sola, A. Moyano, M. A. Pericas and A. Riera, *J. Org. Chem.*, 1999, **64**, 3969; (*d*) M. R. Paleo, I. Cabeza and F. J. Sardina, *J. Org. Chem.*, 2000, **65**, 2108; (*e*) W. A. Nugent, *Org. Lett.*, 2002, **4**, 2133.
3 (*a*) S. Vyskocil, S. Jaracz, M. Smrcina, M. Sticha, V. Hanus, M. Polasek and P. Kocovsky, *J. Org. Chem.*, 1998, **63**, 7727; (*b*) C. Cardellicchio, G. Ciccarella, F. Naso, E. Schingaro and F. Scordari, *Tetrahedron: Asymmetry*, 1998, **9**, 3667; (*c*) C. Cardellicchio, G. Ciccarella, F. Naso, F. Perna and P. Tortorella, *Tetrahedron*, 1999, **55**, 14685; (*d*) G. Bernardinelli, D. Fernandez, R. Gosmini, P. Meier, A. Ripa, P. Schupfer, B. Treptow and E. P. Kundig, *Chirality*, 2000, **12**, 529; (*e*) G. Palmieri, *Tetrahedron: Asymmetry*, 2000, **11**, 3361; (*f*) D.-X. Liu, L.-C. Zhang, Q. Wang, C.-S. Da, Z.-Q. Xin, R. Wang, M. C. K. Choi and A. S. C. Chan, *Org. Lett.*, 2001, **3**, 2733; (*g*) C. Cimarelli, A. Mazzaanti, G. Palmieri and E. Volpini, *J. Org. Chem.*, 2001, **66**, 4759; (*h*) J. Casas, C. Najera, J. M. Sansano and J. M. Saa, *Org. Lett.*, 2002, **4**, 2589; (*i*) B. M. Trost, V. S. C. Yet, H. Ito and N. Bremeyer, *Org. Lett.*, 2002, **4**, 2621.
4 (*a*) M. Betti, *Gazz. Chim. Ital.*, 1906, **36**(II), 392; (*b*) M. Betti, *Org. Synth.*, 1941, **Coll. Vol. I**, 381.
5 W. R. Brode and J. B. Littman, *J. Am. Chem. Soc.*, 1930, **52**, 5056.
6 (*a*) O. Juanes, J. C. Rodriguez-Ubis, E. Brunet, H. Pennemann, M. Kossenjans and J. Martens, *Eur. J. Org. Chem.*, 1999, 3323; (*b*) K. S. Reddy, L. Sola, A. Moyana, M. A. Pericas and A. Riera, *Synthesis*, 2000, 165.
7 (*a*) A. R. Katritzky, *J. Heterocycl. Chem.*, 1999, **36**, 1501; (*b*) A. R. Katritzky, G. Qiu, B. Yang and P. J. Steel, *J. Org. Chem.*, 1998, **63**, 6699; (*c*) A. R. Katritzky, X.-L. Cui, B. Yang and P. J. Steel, *J. Org. Chem.*, 1999, **64**, 1979; (*d*) A. R. Katritzky, G. Qiu, H.-Y. He and B. Yang, *J. Org. Chem.*, 2000, **65**, 3683.
8 H.-P. Husson and J. Royer, *Chem. Soc. Rev.*, 1999, **28**, 383.
9 G. W. Gribble, *J. Org. Chem.*, 1972, **37**, 1833.
10 CCDC reference numbers 183966 (for compound **3b**) and 183965 (for compound **4b**). See http://www.rsc.org/suppdata/p1/b2/b204534f/ for crystallographic files in .cif or other electronic format.
11 M. Daumas, Y. Vo-Quang, L. Vo-Quang and F. Le Goffic, *Synthesis*, 1989, 64.