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New solution free and polymer anchored chiral bispidine-based amino alcohols. Synthesis and screening for the enantioselective addition of diethylzinc to benzaldehyde

Giordano Lesma,* Bruno Danieli, Daniele Passarella, Alessandro Sacchetti and Alessandra Silvani*

Dipartimento di Chimica Organica e Industriale e Centro Interdisciplinare Studi biomolecolari e applicazioni Industriali (CISI), Università degli Studi di Milano, via G. Venezian 21, 20133 Milano, Italy

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Abstract—A new approach has been evaluated for the preparation of solution free and polymer supported chiral bicyclic amino alcohols. This strategy involves the use of readily available starting materials and allows chiral ligands characterised by the bispidine core, bearing a stereogenic centre β to one of the nitrogen atoms to be obtained. The first results obtained from the application of these ligands in the asymmetric addition reaction of diethylzinc to benzaldehyde are discussed.

1. Introduction

One of the most extensively studied methodologies for asymmetric carbon–carbon bond formation is the nucleophilic addition of organometallic reagents to carbonyl compounds. In order to perform these reactions, appropriate chiral ligands must be introduced, with the aim of complexing one or more participants in the reaction.[1] A frequent disadvantage of these enantioselective reactions is that one or more equivalents of chiral ligand have to be used. In fact, some organometallics are able to react with carbonyls even in the absence of a ligand and, in many cases, the rate of complexation between ligand and substrate molecule is slower than the rate of the reaction between uncomplexed substrates. Within this class of reactions, the addition of diethylzinc to aldehydes is one of the few enantioselective reactions involving organometallics in which only catalytic amounts of a chiral agent need to be used to obtain asymmetric induction.[2] In fact, uncoordinated organozinc reactants are virtually inert and the reaction requires a compound coordinating to the metal atom to enhance nucleophilicity. Due to the increased reactivity of the reagent when it is involved in the coordinated complex, a catalytic amount of the ligand can be used. This reaction, affording chiral secondary alcohols, thus provides a yardstick for the efficiency and enantioselectivity of a catalyst. Despite the variety of chiral ligands, mostly bearing a β-amino alcohol moiety,[3] that have been synthesised and tested, the development of cost-effective catalysts exhibiting high reactivity and enantioselectivity remains an active research topic. In particular, the recovery and reuse of chiral ligands or catalysts is an important feature in asymmetric reactions.[4] To this end, polymer anchored molecules have intrinsic advantages in that they can be separated from the products and reused virtually without loss of catalytic activity or enantioselectivity. According to this, many examples of asymmetric catalysts that employ polymer bound chiral ligands have been reported. Even if various chiral 1,2-amino alcohols have been attached to polymers[5] and successfully employed in asymmetric reactions in a heterogeneous system, a persisting drawback is that catalytic activity and enantioselectivity of supported catalysts are usually lower than those recorded with their homogeneous counterparts. As a consequence, continued efforts in this area seem to be fully warranted.

2. Results and discussion

We report here a rapid approach for the solution-phase and solid-phase preparation of bispidine-based amino

* Corresponding authors. Tel.: +39-0250314080; fax: +39-0250314078; e-mail: alessandra.silvani@unimi.it

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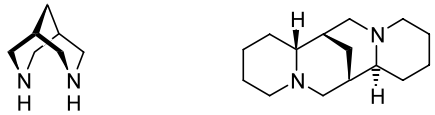
alcohols and their evaluation in asymmetric addition to aldehydes. Bispidine **1** (Fig. 1) is the central bicyclic diaza substructure of the alkaloid sparteine **2**, widely used as efficient ligand in various asymmetric reactions.[6] The diazabicyclo[3.3.1]nonane ring system of bispidine has already been embodied in some different class of chiral ligands,[7] but, to the best of our knowledge, examples of bispidine-based amino alcohols on solid support have not been reported.



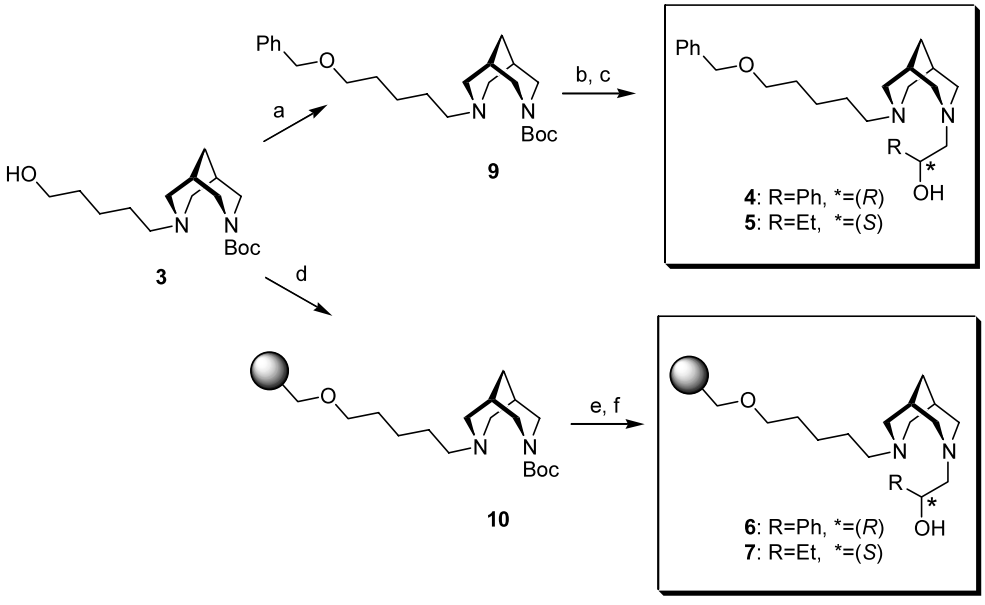
1 **2**

Figure 1.

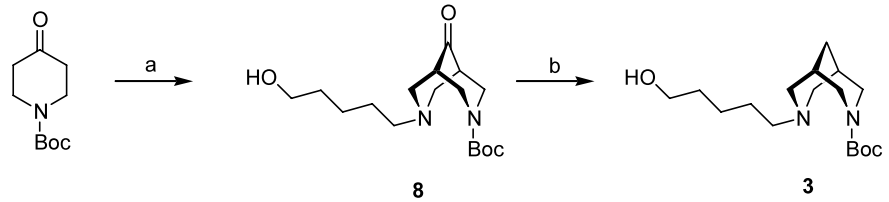
To synthesize differently substituted chiral bispidine amino alcohols, both as free and support-bound ligands, we pursued the two parallel routes shown in Scheme 1. In the preparation of anchored ligands, the first part of the synthesis was performed in solution and then the appropriate scaffold was attached to the support, thus introducing an element of diversity in the ligand molecules in the last step of the sequence.

We envisioned the bispidine **3** as an appropriate starting material, carrying a terminal hydroxyl group as a convenient site for attachment onto the solid support and, at the same time, suitable for easy protection. The chirality is introduced in the last step, after the heterocyclic framework has been built up, by N-alkylation with chiral epoxides. In principle, this scheme allows different ligands to be available from a single resin, by simple variation of the chiral epoxide used in the alkylation process. By means of this strategy, we synthesized the free ligands **4**–**5**, and the corresponding support-bound ligands **6**–**7**, anchored to a chloromethyl-polystyrene (Merrifield resin) polymer backbone. The bicyclic skeleton of **3** was built up in successive transformations starting from *N*-Boc-4-oxo-piperidine and 5-aminopentan-1-ol, via bispidinone **8** (Scheme 2).

The crucial double Mannich reaction to **8** was performed with formaldehyde in MeOH at reflux and proceeded in only 57% yield due to formation of oligomers. The successive deoxygenation of **8** was



Scheme 1. *Reagents and conditions*: (a) NaH, TBAI, BnBr, DMF (93%); (b) 25% TFA, DCM (95%); (c) 2 equiv. of chiral epoxide, toluene, reflux (45–50%); (d) NaH, TBAI, 0.5 equiv. of Merrifield resin, DMF; (e) 20% TFA, DCM 1 h then washing with 25% DIPEA, DCM; (f) *n*-BuLi, THF, 5 equiv. of chiral epoxide.



Scheme 2. *Reagents and conditions*: (a) 5-amino-pentan-1-ol, CH_2O, AcOH, MeOH, reflux (57%); (b) 1. $TsNHNH_2$, EtOH, 2. $NaBH_4$, 4:1 THF/H_2O, then reflux (85%).

accomplished through the reduction of the corresponding tosylhydrazone by means of $NaBH_4$, affording **3** in high yield. The hydroxyl moiety of **3** was then converted either to the benzyl ether **9** or linked onto chloromethylated polystyrene to give polymer **10**. We chose the Merrifield resin, since the contained chloromethyl groups provide a convenient site for O-linkage of our bispidine ligands. Besides, this resin swells efficiently in toluene, which is the solvent of choice in the enantioselective addition of diethylzinc to aldehydes. The linkage was performed by deprotonation of **3** with an excess of sodium hydride in DMF and subsequent reaction of the resulting alkoxide with the Merrifield resin for 12 h. The process of the reaction was monitored by ^{13}C gel-phase NMR (Fig. 2) and the final loading was estimated as about 1.1 mmol g^{-1} (83% loading), from elemental analysis data.

Removal of the Boc group from **9** and **10** yielded the corresponding N–H compounds, which were N-alkylated with the chiral epoxides (*R*)-styrene oxide and (*S*)-1,2-epoxybutane. In order to obtain the desired regiochemistry, solution phase ring opening reactions were carried out thermically in refluxing toluene to give the final products **4** and **5** in moderate yields. On the other hand, the supported ligands **6**–**7** were obtained by deprotonation of the nitrogen with BuLi in THF and quenching of the anion with the epoxide. In order to achieve a quantitative conversion, five equivalents of the chiral epoxide were used. Also in this case the ring opening proceeds with complete regioselectivity, to afford amino alcohols **6** and **7** in high yields. In the case of solid-phase reactions, the yields were determined by gravimetric and elemental analyses and the expected structures of ligands **6** and **7** were confirmed by ^{13}C gel-phase NMR. Enantiopurity of soluble ligands **4** and **5** was confirmed by comparison with the corresponding racemic compounds, by means of chiral HPLC.

The activity of the ligands was then tested in the enantioselective addition of diethylzinc to benzaldehyde (Table 1). The reaction was carried out in toluene at 0°C with 10% mol of ligand and two equivalents of diethylzinc.

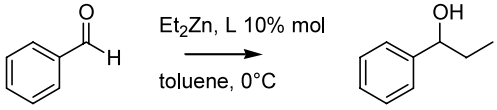


Table 1.

Entry	Ligand	Yield (%)[a]	E.e. (%)[b]	Config.[b]
1	**4**	94	96	*R*
2	**5**	93	35	*S*
3	**6**	95	25	*R*
4	**7**	95	5	*S*

[a] Isolated yield.
[b] Determined by HPLC (see Section 4).

Excellent enantioselectivity could be achieved by employing the free solution ligand **4** (entry 1). The comparison with the 35% e.e. obtained with the ligand **5** (entry 2) highlights the necessity of a bulky group on the stereocentre of the ligand in order to achieve high e.e. Supporting of these ligands (entries 3 and 4) results in a drastic lowering of the e.e. However, in all cases the high conversions of benzaldehyde to the secondary

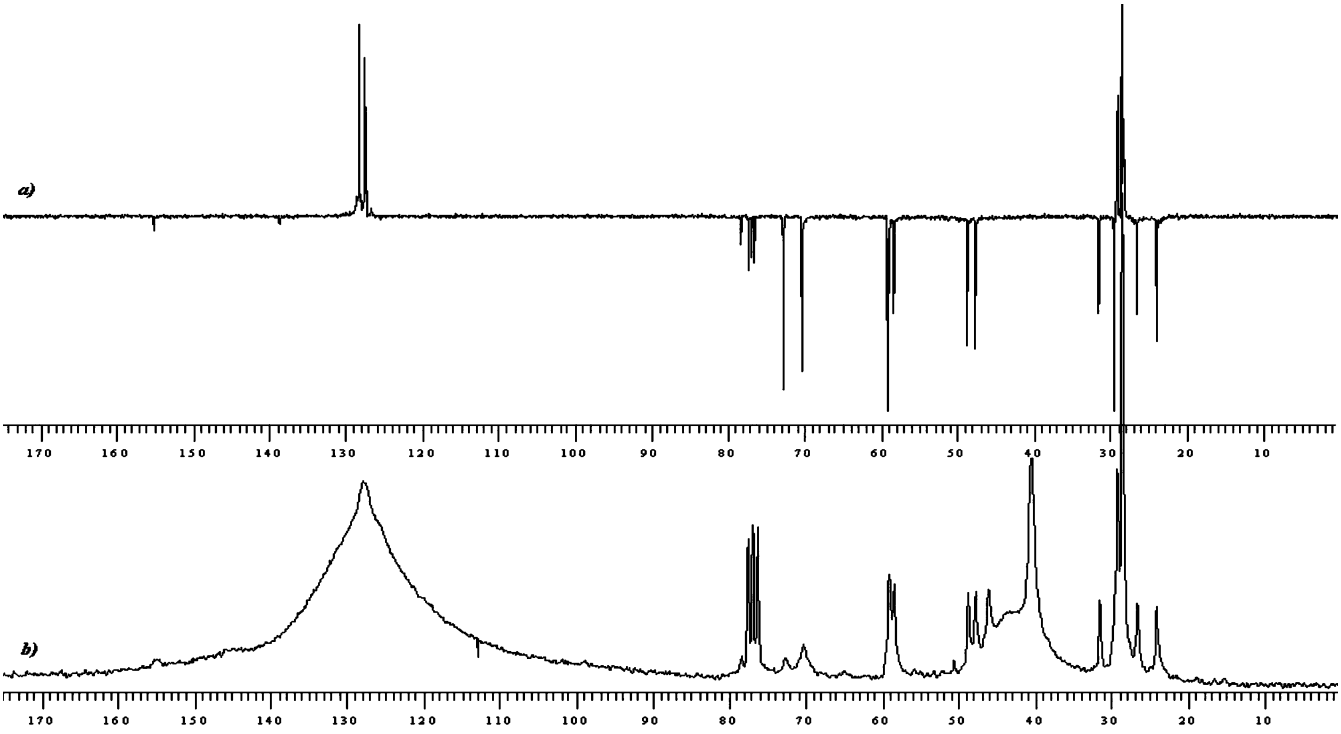


Figure 2. Comparison between ^{13}C NMR-APT spectrum of compound **9** (*a*) and ^{13}C NMR gel-phase of polymer **10** (*b*).

alcohol demonstrate the good activity of both the solution free and the polymer supported ligands. This confirms the chelating ability of these compounds even when supported onto an insoluble polymer matrix. Notably, the configuration of the addition product is the same as the aminoalcohol ligand, in accord to the model proposed by Noyori[3] for which an (*R*)-aminoalcohol leads to an (*R*)-product and vice versa. This rule is also followed by the supported ligands.

3. Conclusions

In conclusion, we performed an easy and enantioselective synthesis of solution free and polymer supported chiral bispidine-based aminoalcohols. The results obtained from the application of the new chiral ligands in a model reaction—the diethylzinc addition to benzaldehyde—are good in terms of conversion (with high e.e. for the homogeneous ligand **4** and modest e.e. for the heterogeneous ones). Studies are in progress to improve the supported ligands' activity by changing the type of solid support and linker or, alternatively, the anchoring site of the molecule. Moreover, this ligand family, being equipped with O and N as chelating atoms, will be exploited in other asymmetric reactions involving different transition metals, such as Cu, Sn, Ti, Sc, Ni and lanthanides.

4. Experimental

4.1. General

All solvents were distilled and properly dried, when necessary, prior to use.—During usual workup, all organic extracts were dried (Na_2SO_4 or $MgSO_4$) and evaporated.—All reactions were monitored by thin layer chromatography (TLC) on precoated silica gel 60 F_{254} (Merck); spots were visualized with UV light or by treatment with 1% aqueous $KMnO_4$ solution. Products were purified by flash chromatography (FC) on Merck silica gel 60 (230–400 mesh).—^1H and ^{13}C NMR spectra were recorded with Bruker AC 300 (^1H, 300 MHz; ^{13}C, 75.4 MHz) spectrometer in $CDCl_3$ solutions (if not otherwise stated) with TMS as internal standard.—HR, EI (70 eV) and FAB mass spectra in the positive mode, were measured on VG 70–70 EQ–HF instrument equipped with its standard sources.—Optical rotations were measured with Perkin–Elmer 241 polarimeter.—Analytical liquid chromatography was carried out with a Kontron HPLC system equipped with a UV detector and a Chiracel OD HPLC column

4.2. Preparation of ligands 4–7

4.2.1. 3-*tert*-Butyloxycarbonyl-7-(5-hydroxypentyl)-9-oxo-3,7-diazabicyclo[3.3.1]nonane, 8. To a solution of 5-aminopentan-1-ol (550 mg, 5 mmol) in 20 ml of dry methanol, acetic acid (0.29 ml, 5 mmol), hydrochloric acid (0.21 ml, 2.5 mmol) and paraformaldehyde (312 mg, 10 mmol) were added. To the refluxing reaction mixture a solution of *N*-Boc-4-oxo-piperidine (1 g, 5 mmol) in dry methanol was slowly added. After 3 h the reaction was cooled to room temperature and the solvent was evaporated in vacuo. The residue was treated with 20 ml of a 5 M ammonia solution and then extracted with AcOEt. After evaporation of the solvent, the crude product was purified by flash chromatography on silica gel (AcOEt/hexane 7/3, as eluant) to yield the product **8** as a yellow oil (928 mg, 57%). ^1H NMR (200 MHz, DMSO, 140°C): δ 4.33 (d, $J=13$ Hz, 2H), 3.45 (t, $J=6$ Hz, 2H), 3.29 (dd, $J=13$ Hz, $J=5$ Hz, 2H), 3.11 (dd, $J=12$ Hz, $J=2$ Hz, 2H), 2.67 (dd $J=12$ Hz, $J=5$ Hz, 2H), 2.50 (m, 2H), 2.30 (t, $J=7$ Hz, 2H), 1.80 (s, 1H), 1.48–1.25 (m, 15H). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 213.51, 154.87, 79.83, 62.44, 59.78, 58.18, 57.25, 50.65, 49.81, 47.92, 32.58, 28.47, 26.68, 23.56. MS (EI) m/z (%): 326 (51) [M^+].

4.2.2. 3-*tert*-Butyloxycarbonyl-7-(5-hydroxypentyl)-3,7-diazabicyclo[3.3.1]nonane, 3. To a solution of bispidinone **10** (3.33 g, 10.2 mmol) in 50 ml of ethanol, tosylhydrazine (2.29 g, 12.3 mmol) was added. The reaction was refluxed for 3 h, then the solvent was evaporated. To the crude tosylhydrazone derivative, dissolved in 50 ml of THF–water 4:1 and cooled to 0°C, $NaBH_4$ (3.78 g, 0.1 mol) was slowly added. The solution was stirred overnight at rt, then it was refluxed for 2 h. After cooling at rt, water was added and the mixture was extracted with AcOEt. Evaporation of the solvent afforded an oil which was purified by flash chromatography on silica gel (AcOEt/hexane 7/3, as eluant) to yield the desired product **3** (2.71 g, 85%). ^1H NMR (300 MHz, DMSO, 140°C): δ 3.95 (d, $J=13.8$ Hz, 2H), 3.44 (t, $J=6.0$ Hz, 2H), 3.08 (dd, $J=13.8$ Hz, $J=3.8$ Hz, 2H), 2.88 (d, $J=11.3$ Hz, 2H), 2.21 (d, $J=11.3$ Hz, 2H), 2.18 (t, $J=7.7$ Hz, 2H), 1.83 (m, 2H), 1.64–1.59 (m, 2H), 1.48–1.25 (m, 15H). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 155.20, 78.68, 62.43, 58.64, 57.83, 57.59, 48.73, 47.65, 32.65, 31.36, 29.00, 28.55, 26.36, 23.25. MS (EI) m/z (%): 312 (15) [M^+].

4.2.3. 3-*tert*-Butyloxycarbonyl-7-(5-benzyloxypentyl)-3,7-diazabicyclo[3.3.1]nonane, 9. The bispidine **3** (4.24 g, 13.6 mmol), TBAI (502 mg, 1.36 mmol) and NaH (391 mg, 16.3 mmol) in 90 ml of dry THF were stirred under a nitrogen atmosphere. After 30 min, benzyl bromide (1.62 ml, 13.6 mmol) was added. The reaction was stirred overnight. Then water was added and the mixture was extracted with AcOEt. The obtained solution was treated with 10 g of Floresil, filtered and the filtrate was washed with AcOEt. The combined organic layers were dried and evaporated yielding the pure product **9** (5.10 g, 93%). ^1H NMR (300 MHz, DMSO, 140°C): δ 7.35 (m, 5H), 4.47 (s, 2H), 3.95 (d, $J=13.8$ Hz, 2H), 3.44 (t, $J=6.0$ Hz, 2H), 3.08 (dd, $J=13.8$ Hz, $J=3.8$ Hz, 2H), 2.88 (d, $J=11.3$ Hz, 2H), 2.21 (d, $J=11.3$ Hz, 2H), 2.18 (t, $J=7.7$ H, 2H), 1.83 (m, 2H), 1.64–1.59 (m, 2H), 1.48–1.25 (m, 15H). ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 155.15, 138.69, 128.29, 127.58, 127.45, 78.44, 72.84, 70.46, 59.26, 59.08, 58.44, 48.81, 47.77, 31.63, 29.69, 29.28, 29.18, 28.65, 26.65, 24.09. MS (EI) m/z (%): 402 (34) [M^+].

4.2.4. (*R*)-2-[7-(5-Benzyloxypentyl)-3,7-diazabicyclo-[3.3.1]non-3-yl]-1-phenylethanol, 4. The starting material **9** (1.15 g, 2.86 mmol) was dissolved in a 20% TFA/DCM solution and stirred for 1 h. A 5 M ammonia solution

was added to pH 9–10 and the aqueous phase was extracted with DCM. The combined organic layers are dried and evaporated, to yield the desired free amine (820 mg, 2.70 mmol) in 95% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.30 (m, 5H), 4.47 (s, 2H), 3.48 (t, $J=6.0$ Hz, 2H), 3.39 (d, $J=13.0$ Hz, 2H), 3.12 (d, $J=13.0$ Hz, 2H), 2.42 (d, $J=12.0$ Hz, 2H), 2.33 (d, $J=12.0$ Hz, 2H), 2.29 (t, $J=7.7$ Hz, 2H), 2.09 (m, 2H), 1.64–1.59 (m, 2H), 1.40–1.25 (m, 6H). ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 138.57, 128.29, 127.58, 127.45, 72.80, 69.98, 58.36, 49.51, 30.74, 29.45, 27.09, 26.18, 23.94. MS (EI) m/z (%): 402 (29) [M$^+$].

The obtained amine (1.22 g, 4.02 mmol) was dissolved in 5 ml of dry toluene, then (*R*)-styrene oxide (0.505 ml, 4.42 mmol) was added. The mixture was refluxed for 24 h. After cooling, the solution was treated with 2 ml of HCl 1N and stirred for 30′. Then, 5 M ammonia solution was added until pH 9–10 and the aqueous phase was extracted with AcOEt. After drying and evaporating the solvent, the obtained crude product was purified by flash chromatography on silica gel (AcOEt/MeOH/TEA 78/19/3 as eluant), to afford **4** in 45% yield (766 mg, 1.81 mmol). $[\alpha]_D^{20}=-82$ ($c=0.33$, EtOH); ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.35 (m, 10H), 4.73 (dd, $J=10.5$ Hz, $J=4.5$ Hz, 1H), 4.48 (s, 2H), 3.49 (t, $J=6.0$ Hz, 2H), 3.10–2.20 (m, 12H), 1.83 (m, 2H), 1.65 (m, 2H), 1.60–1.30 (m, 6H). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 143.33, 138.74, 128.29, 128.12, 127.60, 127.38, 126.95, 125.87, 72.84, 70.43, 69.04, 64.52, 60.03, 59.15, 54.64, 32.47, 30.66, 29.60, 26.28, 24.32. MS (EI) m/z (%): 422 (17) [M$^+$].

4.2.5. (*S*)-2-[7-(5-Benzyloxypentyl)-3,7-diazabicyclo-[3.3.1]non-3-yl]butan-2-ol, 5. The same procedure as for **4** was followed, except that (*S*)-1,2-epoxybutane (345 μl, 4.01 mmol) was used. The product **5** was obtained with 50% yield (544 mg 1.45 mmol). $[\alpha]_D^{20}=+36$ (*c* 0.33, EtOH) ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.35 (m, 5H), 4.48 (s, 2H), 4.05 (m, 1H), 3.49 (t, $J=6.0$ Hz, 2H), 3.10–2.30 (m, 10H), 2.18 (t, $J=7.7$ Hz, 2H), 1.83 (m, 2H), 1.65 (m, 2H), 1.60–1.30 (m, 8H), 0.94 (s, $J=8.0$ Hz, 3H). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 138.58, 128.35, 127.65, 127.49, 72.88, 70.33, 67.35, 62.09, 59.53, 59.21, 50.78, 31.95, 29.52, 28.42, 28.18, 26.52, 24.07, 11.43. MS (EI) m/z (%): 374 (14) [M$^+$].

4.2.6. Coupling of ligand precursor 3 to the solid phase. The bispidine **3** (645 mg, 2.07 mmol), TBAI (78 mg, 0.21 mmol) and NaH (60 mg, 2.48 mmol) in 30 ml of dry THF were stirred under a nitrogen atmosphere. After 30 min, Merrifield resin (837 mg, 1.03 mmol, loading 1.23 mmol/g) was added. The reaction was mechanically stirred overnight. Then the resin was filtered and washed with MeOH and DCM twice (83% loading from elemental analysis data).

4.2.7. Cleavage of the Boc protecting group on solid support. The resin **10** was suspended in a 20% TFA/DCM solution in a fritted filtration syringe and mechanically stirred. After 3 h the solution was filtered and the resin was washed three times with a 20% DIPEA/DCM solution and then with MeOH and DCM twice.

4.2.8. General procedure for chiral epoxide ring opening on solid phase: preparation of 6 and 7. Under a nitrogen atmosphere the resin was suspended in 5 ml of dry THF in a fritted filtration syringe. After cooling to 0°C, butyllithium was added (1.6 M in hexane, 2 equiv.). The reaction was mechanically stirred for 1 h, then the temperature was raised to room temperature. The chiral epoxide (5 equiv.) was added and the mixture was mechanically stirred overnight. Then the resin was filtered and washed with MeOH and DCM twice.

4.2.9. General procedure for the addition of diethylzinc to benzaldehyde in presence of the ligands. To a solution of benzaldehyde (1 equiv.) in dry toluene, the ligand (10% mol, 0.1 equiv.) was added. To the mixture cooled to 0°C, diethylzinc was added (1 M in hexane, 2 equiv.). The reaction was allowed to warm to room temperature overnight then it was quenched with 1 M HCl. The aqueous phase was extracted with AcOEt. After drying and evaporating the solvent, the crude product was used for HPLC analysis to determine the enantiomeric excess (Chiracell OD column with 2.5% propan-2-ol in hexane as eluant and 0.600 ml/min flow: retention times of 18′ for the (*R*)-enantiomer and 21′ for the (*S*)-enantiomer, see Table 1).

Acknowledgements

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References

1. *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; John Wiley & Sons, Inc., Publ., New York, 2000
2. Soai, K.; Niwa, S. *Chem. Rev.* **1992**, *92*, 833–856.
3. (a) Noyori, R.; Kitamura, M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 49–70; (b) Bolm, C.; Schlingloff, G.; Harms, K. *Chem. Ber.* **1992**, *125*, 1191–1203.
4. Fan, Q.-H.; Li, Y.-M.; Chan, A. S. C. *Chem. Rev.* **2002**, *102*, 3385–3466.
5. (a) Vidal-Ferran, A.; Bampos, N.; Moyano, A.; Pericàs, M. A.; Riera, A.; Sanders, J. K. M. *J. Org. Chem.* **1998**, *63*, 6309; (b) Liu, G.; Ellmann, J. A. *J. Org. Chem.* **1995**, *60*, 7712; (c) Watanabe, M.; Soai, K. *J. Chem. Soc., Perkin Trans. 1* **1994**, 837; (d) Soai, K.; Watanabe, M.; Yamamoto, A. *J. Org. Chem.* **1990**, *55*, 4832; (e) Itsuno, S.; Fréchet, J. M. J. *J. Org. Chem.* **1987**, *52*, 4140.
6. (a) Hoppe, D.; Hense, T. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2282–2316; (b) Beak, P.; Basu, A.; Gallagher, D. J.; Park, Y. S.; Thayumanavan, S. *Acc. Chem. Res.* **1996**, *29*, 552–560; (c) Schwerdtfeger, J.; Hoppe, D. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1505–1507; (d) Muci, A. R.; Campos, K. R.; Evans, D. A. *J. Am. Chem. Soc.* **1995**, *117*, 9075–9076; (e) Curtis, M. D.; Beak, P. *J. Org. Chem.* **1999**, *64*, 2996–2997; (f) Denmark, S. E.; Stiff, C. M. *J. Org. Chem.* **2000**, *65*, 5875–5878; (g) Hodgson, D. M.;

Norsikian, S. L. M. *Org. Lett.* **2001**, *3*, 461–463; (h) Sigman, M. S. *J. Am. Chem. Soc.* **2001**, *123*, 7475–7476.

7. (a) Haack, K. J.; Goddard, R.; Porschke, K. R. *J. Am. Chem. Soc.* **1997**, *119*, 7992–7999; (b) Park, Y. S.; Weisenburger, G. A.; Beak, P. *J. Am. Chem. Soc.* **1997**, *119*, 10537–10538; (c) Park, Y. S.; Weisenburger, G. A.; Beak, P. *J. Am. Chem. Soc.* **1997**, *119*, 10537–10538; (d) Huttenloch, O.; Laxman, E.; Waldmann, H. *Chem. Commun.* **2002**, 673; (e) Huttenloch, O.; Spieler, J.; Waldmann, H. *Eur. J. Org. Chem.* **2000**, *6*, 391–399; (f) Huttenloch, O.; Laxman, E.; Waldmann, H. *Chem. Eur. J.* **2002**, *20*, 4767–4780.