Tetrahedron 66 (2010) 743–749

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Synthesis of new bis-BINOL-2,2′-ethers and bis-H_8BINOL-2,2′-ethers evaluation of their Titanium complexes in the asymmetric ethylation of benzaldehyde

Artur R. Abreu [a,b], Mariette M. Pereira [a,*], J. Carles Bayón [b,*]

[a] Departamento de Química, Universidade de Coimbra, Rua Larga 3004-535, Coimbra, Portugal
[b] Departament de Química, Universitat Autònoma de Barcelona, Bellaterra 08193 Barcelona, Spain

ARTICLE INFO

Article history:
Received 4 October 2009
Received in revised form 9 November 2009
Accepted 10 November 2009
Available online 3 December 2009

ABSTRACT

The preparation by means of different synthetic paths of a series of bis-BINOL and bis-H_8BINOL ligands is described. The ligands consist of two BINOL or H_8BINOL fragments, joined by diverse linkages through the oxygen at the 2′-position of the arylic fragments. These ligands were applied to the Ti(O^iPr)$_4$ catalyzed asymmetric alkylation of benzaldehyde with Et_2Zn. The performance of these catalysts is very sensitive to the nature of the ether linkage. The ligand with a propylene link shows better enantioselectivity (ca. 70%) than those with two or four carbon atoms joining the BINOL fragments. Furthermore, using the propylene link, but replacing (*R*)-BINOL by (*R*)-H_8BINOL, a significant improvement in the stereoselectivity of the catalysts was achieved (ca. 80% ee in (*R*)-1-phenylpropan-1-ol). A cooperative effect was observed between the chirality at the BINOL fragment and that of a (*S*,*S*)-4,5-bis(methylene)-2,2-dimethyl-1,3-dioxolane link, derived from tartaric acid. When this chiral link combines with two (*S*)-BINOL fragments, the alkylation of benzaldehyde in toluene produces 70% ee of (*S*)-1-phenylpropan-1-ol, while the (*R*)-BINOL derivative ligand with the same link, in identical conditions, yields only 40% ee of the (*R*)-alcohol.

1. Introduction

Over the last thirty years, the number of new chiral ligands developed to be used in asymmetric catalysis has grown exponentially. However, only a limited number of those ligands have been applied across a wide range of catalytic asymmetric transformations. One of them is the axially chiral 1,1′-bi-2-naphthol (BINOL)[1,2] and its derivatives that form highly enantioselective catalysts with main group elements, transition metals and f-block elements, as well as with heterobimetallic combinations from these groups.[3–9]

Among the countless examples of metal complexes of BINOL used as asymmetric catalysts, a key role is played by the Ti(IV) complexes family.[10]

Catalysts containing partially hydrogenated BINOL ligands, 5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-bi-2-naphthol (H_8BINOL),[11] and 5,6,7,8-tetrahydro-1,1′-bi-2-naphthol (H_4-BINOL),[12] very often exhibited better stereoselectivity than those obtained from the corresponding BINOL catalysts.[13,14] This has been attributed to the steric and electronic modulation produced by the saturated fragment in the binaphthyl backbone.[15,16] When two BINOL fragments are linked through different groups, the resulting entities are normally described as bis-BINOL derivatives. Shibasaki et al. reported a novel class of bis-BINOL ligands, in which two BINOL units are linked through the 3,3′-positions by carbon, oxygen or sulfur bridges. These ligands offered new possibilities for multifunctional asymmetric catalysts.[7,17–19] Other 3,3′-bis-BINOL derivatives containing bipyridine[20] and diyne[21] as linking groups have been applied as agents for molecular recognition.

More recently, a family of bis-BINOL ligands, consisting of two 2-hydroxy-1,1′-binaphthalenes joined through the 2′-positions by a di-ether linkage, was synthesized with moderate overall yield (30–40%).[22] Surprisingly, these appealing ligands have never been used in asymmetric catalysis.

Enantioselective carbon–carbon bond formation is one of the most important types of bond construction in organic synthesis.[23] The asymmetric alkylation of aromatic aldehydes with diethylzinc, catalyzed by titanium complexes of *N*-sulfonylated β-amino-acids,[24a–c] and specially BINOL derivatives[24d] is a well known reaction which has quite often been used to evaluate the performance of new ligands in asymmetric catalysis. Since it is assumed that the binuclear catalyst [Ti_2(BINOLate)(O^iPr)$_6$] is the active species in stereoselective alkylation of aldehydes, it would be of great interest to evaluate the performance of some bis-BINOL ligands in this reaction. Therefore, herein we report several synthetic approaches for the synthesis of a variety of bis-BINOL ligands

* Corresponding authors. Tel.: +351 239854474; fax: +351 239827703.
E-mail address: mmpereira@qui.uc.pt (M.M. Pereira).

0040-4020/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2009.11.047

featuring a carbon linker of different length and structure connecting the hydroxyl groups of two BINOL units or their partially hydrogenated counterpart.

The performance of the titanium complexes of these new ligands in the asymmetric ethylation of benzaldehyde with diethylzinc is also described. A significant influence of the size and structure of the ether bridge as well as the partial reduction of BINOL was observed in the outcome of this reaction.

2. Results and discussion

2.1. Ligand synthesis

Two different synthetic strategies have been used to synthesize a library of bis-BINOL ethers:

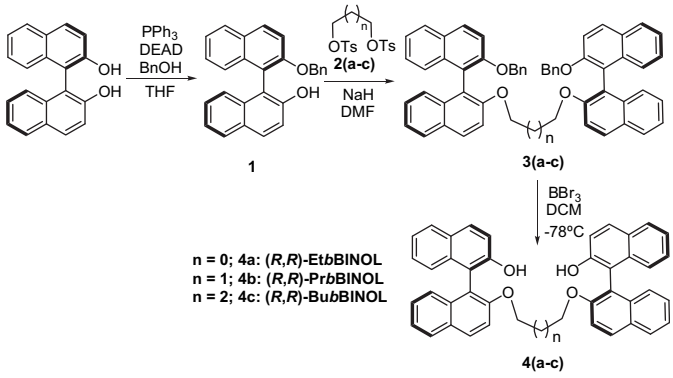
(i) monoprotection of BINOL or H_8BINOL via modified Mitsunobu reaction,[25,26] followed by coupling with the desired ditosyl derivative, and subsequent hydroxyl deprotection (Schemes 1, 2 and 5).
(ii) formation of BINOL-stannylene acetal,[27,28] followed by reaction with activated alkyl halides (Scheme 3).

In the first approach, BINOL was coupled with benzyl alcohol via slight modifications of Mitsunobu reaction[26], in the presence of PPh_3 and diethyl azodicarboxylate (DEAD) at room temperature, for 48 h. After chromatographic purification, 2′-(benzyloxy)-1,1′-binaphthyl-2-ol, (*R*)-BnBINOL, (***R***)-**1**, was isolated with 86% yield (Scheme 1).

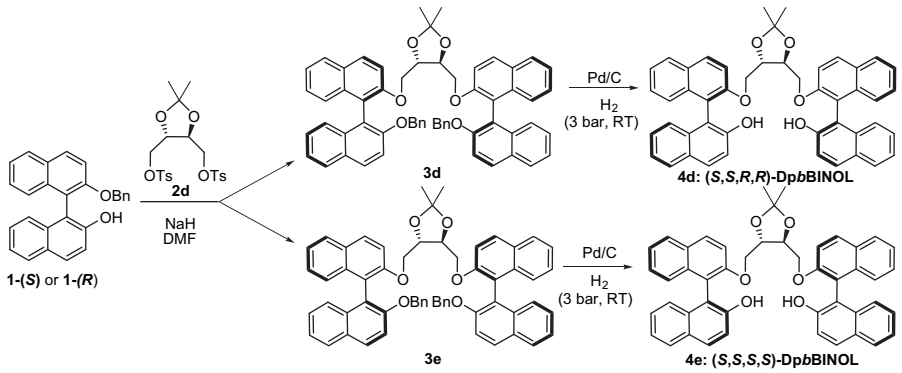
In order to modulate the size and steric hindrance of the ether bridge, ditosyl ethers with different chain size were prepared from the coupling of the correspondent diol with toluene-4-sulfonyl chloride in THF/H_2O solution, according to previously described procedure, yielding the desired ditosyl derivatives **2a**–**d**.[29] Subsequently, to a solution of (*R*)-BnBINOL and NaH in DMF, the desired ditosyl derivative, namely 1,2-ditosylethane **2a**, 1,3-ditosylpropane **2b** or 1,4-ditosylbutane **2c**, was added. After 6 h at 80 °C, the ethers **3a**–**c** were obtained with good yields, **3a** 71%, **3b** 85% and **3c** 93% (Scheme 1).

Hydrogenolysis of **3a**–**c** over Pd/C (5%) in isopropanol/ethyl acetate under 3 bar of H_2 at 25 °C gave (*R*,*R*)-1,2-bis{2′(2-hydroxy-1,1′-binaphthyl)oxy}ethane (*R*,*R*)-Et*b*BINOL **4a** (42% yield), (*R*,*R*)-1,3-bis{2′(2-hydroxy-1,1′-binaphthyl)oxy}propane Pr*b*BINOL **4b** (58% yield), and (*R*,*R*)-1,4-bis{2′(2-hydroxy-1,1′-binaphthyl)oxy}-butane (*R*,*R*)-Bu*b*BINOL **4c** (62% yield). All the attempts to improve the yield of the hydrogenolysis step by increasing the pressure or temperature failed, due to the partial hydrogenation of the aromatic rings.[30] In order to improve the overall deprotection yield, the ethers **3a**–**c** were dissolved in CH_2Cl_2 and treated with a slight excess of BBr_3 at −78 °C.[30,31] After work-up and chromatographic purification, enantiomerically pure (*R*,*R*)-Et*b*BINOL **4a** and (*R*,*R*)-Pr*b*BINOL **4b**, (*R*,*R*)-Bu*b*BINOL **4c** were obtained with 80%, 78% and 82% yield, respectively, (Scheme 1). Therefore, through this improved route the three compounds could be isolated in 70% overall yield based on BINOL, while with the previously reported dihydropyran protection approach, overall yields around 40% were reported.[22]

In order to evaluate the cooperative effect between the chirality at the BINOL fragments and that of the link, new dihydroxydiether type ligands were prepared from the ditosylate derivative **2d**.[32] The coupling of **2d** with **1**-(***S***) or **1**-(***R***) (Scheme 2), under the conditions described for **3**(**a**–**c**), yields the diatereoisomeric ethers **3**(**d**–**e**) (ca. 70% yield). Due to the acetal weakness toward acid media, the BBr_3 deprotection was not applied in the case of **3**(**d**–**e**). Hydrogenolysis optimization was carried out using similar conditions to those described for **3a**–**c**, yielding (*R*,*R*)-2′,2″-((4*S*,5*S*)-2,2-dimethyl-1,3-



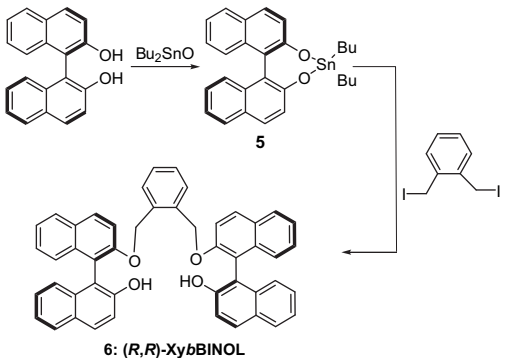
Scheme1. Synthesis of precursors and bis-BINOL-2,2′-ethers holding alkyl bridges of different carbon chain length.



Scheme 2. Synthesis of precursors and bis-BINOL-2,2′-ethers holding a chiral bridge.

dioxolane-4,5-diyl)bis(methylene)-bis(oxy)di-1,1′-binaphthyl-2-ol, (*S*,*S*,*R*,*R*)-Dp*b*BINOL **4d**, (65%), and (*S*,*S*)-2′,2″-((4*S*,5*S*)-2,2-dimethyl-1,3-dioxolane-4,5-diyl)-bis-(methylene)bis(oxy)di-1,1′-binaphthyl-2-ol, (*S*,*S*,*S*,*S*)-Dp*b*BINOL **4e**, (64%) (Scheme 2).

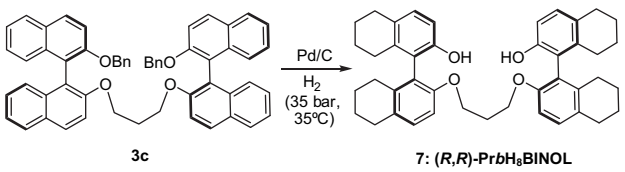
The synthesis of a bis-BINOL-2,2′-ether containing a *o*-xylene bridge required another synthetic strategy, since the benzyl deprotection, described above, would also cleave the *o*-xylene bridge. So, in a second approach, BINOL was converted into its tin acetal **5**, via reaction with dibutyltin oxide in refluxing 1,2-dichloroethane, with concomitant removal of water using a Dean–Stark head. It should be noted that in this approach the formation of the tin acetal is the critical step in the overall yield of the desired bis-BINOL ethers. To avoid some of the irreproducibility of previously described procedures,[28,33] the reaction was followed by IR spectroscopy, until complete disappearance of the characteristic stretching OH band (3500 cm^{-1}) was observed. After evaporation of the solvent, the crude BINOL-stannylene acetal **5**, was reacted in toluene, without further purification, with 1,2-bis-(bromomethyl)benzene. Better yields were achieved by adding catalytic amounts of NBu_4I to the reaction, to generate the corresponding diiodo derivative in situ.[34] The reaction was followed by TLC and quenched after 72 h, yielding α,α′-bis[2′(2-hydroxy-1,1′-binaphthyl)oxy]-*o*-xylene ((*R*,*R*)-Xy*b*BINOL) **6** with 25% yield.



Scheme 3. Synthesis of (*R*,*R*)-Xy*b*BINOL via tin acetal formation.

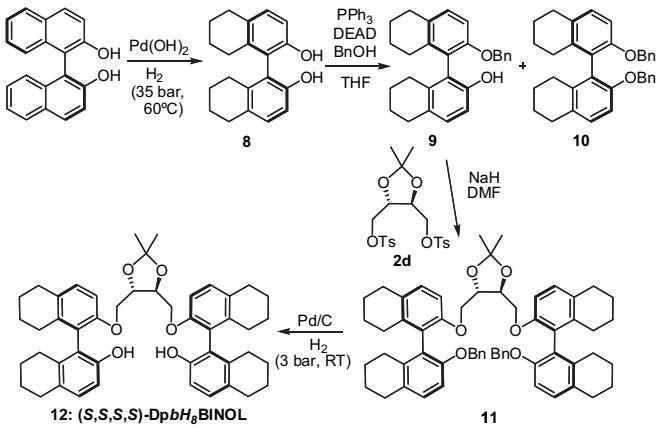
This result prompted us to replace the 1,2-bis(bromomethyl)benzene by the isolated iodo derivative, prepared by reaction of 1,2- bis(bromomethyl)benzene with NaI in acetone. Thus, refluxing **5** with 1,2-bis(iodomethyl)-benzene, (*R*,*R*)-Xy*b*BINOL **6** was obtained in 40% yield (Scheme 3).

It was previously described that H_8BINOL showed higher asymmetric induction than BINOL in the alkylation reaction of aldehydes catalyzed by titanium complexes.[13b] Therefore, to study the effect of the partial hydrogenation of binaphtyl ring, we carried out the hydrogenation of **3b** in the presence of H_2 (35 bar, 35 °C) using Pd/C (5%) as catalyst. In these reaction conditions, the hydrogenolysis of benzyl group takes places together with the hydrogenation of external aromatic phenyl ring, producing (*R*,*R*)-1,3-bis{2′(5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-bibenzobenzen-2-ol)oxy}propane (*R*,*R*)-Pr*b*H_8BINOL **7**, yielding, 80% after chromatographic purification (Scheme 4).



Scheme 4. Synthesis of (*R*,*R*)-Pr*b*H_8BINOL.

When the previous approach was applied to the synthesis of (*S*,*S*,*S*,*S*)-Dp*b*H_8BINOL (Scheme 5), a complex mixture of products was obtained. To overcome this difficulty, another synthetic strategy was implemented. Thus, (***S***)-BINOL was transformed into (*S*)-H_8BINOL (Scheme 5), accordingly to the previously described partial hydrogenation over $Pd(OH)_2$ (35 bar, 60 °C, 72 h). (*S*)-H_8BINOL **8** was coupled with benzyl alcohol via slight modifications of Mitsunobu reaction, at room temperature, for 48 h.[26] After chromatographic purification, 2′-(benzyloxy)-4a,5,5′,6,6′,7,7′,8,8a,8′-decahydro-1,1′-binaphthyl-2-ol, (*S*)-BnH_8BINOL, (***S***)-**9**, was isolated in 80% yield.



Scheme 5. Synthesis of precursors and bis-H_8BINOL-2,2′-ethers holding a chiral bridge.

In contrast with the previously described selective monoprotection of BINOL, in this case, the corresponding dibenzyl product **10**, was obtained as side-product (10% yield). (Scheme 5) However, this impurity can be easily separated by column chromatography.

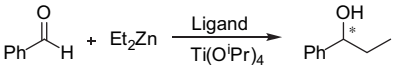
Subsequently, to a solution of (***S***)-**9** and NaH in DMF, the ditosyl derivative **2d** was added and kept at 70 °C along 10 h. After silica gel column chromatography **11** was isolated with 81% yield. After deprotection, using the hydrogenolysis procedure described above, the (1*S*,1″*S*)-2′,2″-((4*S*,5*S*)-2,2-dimethyl-1,3-dioxolane-4,5-diyl)-bis(methylene)bis(oxy)bis(5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl-2-ol) **11** was obtained in 68% yield.

2.2. Catalytic asymmetric ethylation of aldehydes

The alkylation of benzaldehyde with Et_2Zn catalyzed by $Ti(O^iPr)_4$, in the presence of the ligands **4**(**a**–**c**), was used to evaluate the influence of the carbon chain length of the bridge between the two hydroxynaphthyl fragments on the performance of the catalyst (Table 1, entries 1–6). It is well established that the solvent can have an important effect not only on the reaction rate, but also on the enantioselectivity of the process.[10] Therefore, the reactions were carried out both in toluene (PhMe) and dichloromethane (DCM). In all the experiments conversions were lower in dichloromethane (47–93%) than in toluene (85–99%), while only moderate differences in the enantioselectivities were observed (Table, entries 1–6). From these results, it is noteworthy that the ligand with the propylene bridge, (*R*,*R*)-Pr*b*BINOL, yields the most active and stereoselective catalyst, in both solvents, 62% ee in toluene and 69% ee in dichloromethane (Table 1, entries 3 and 4).

In order to assess the influence of the rotation around C2–C3 carbons atoms of the di-ether link fragment, we pursued the studies of the catalytic alkylation of benzaldehyde using ligands **4d**–**e** and **6** containing a ring in the link that hampers the free rotation of the bridge chain. The catalytic reactions using (*R*,*R*)-Xy*b*BINOL **6** or the (*S*,*S*,*R*,*R*)-Dp*b*BINOL **4d** gave moderate ee in both solvents (ca. 40% in the (*R*) product), similar to that observed with

Table 1
Asymmetric ethylation of benzaldehyde[a] with Et_2Zn catalyzed by $Ti(O^iPr)_4$ and bis-BINOL-2,2′-ethers ligands, **4a**–**e**,**6**,**7**, and **12**



Entry	Ligand	Solv.	Conv[b] (%)	ee (%)
1	(*R*,*R*)-Et*b*BINOL (**4a**)	PhMe	89	46 (*R*)
2		DCM	47	41 (*R*)
3	(*R*,*R*)-Pr*b*BINOL (**4b**)	PhMe	99	62 (*R*)
4		DCM	93	69 (*R*)
5	(*R*,*R*)-Bu*b*BINOL (**4c**)	PhMe	87	49 (*R*)
6		DCM	48	44 (*R*)
7	(*R*,*R*)-Xy*b*BINOL (**6**)	PhMe	98	44 (*R*)
8		DCM	79	40 (*R*)
9	(*S*,*S*,*R*,*R*)-Dp*b*BINOL (**4d**)	PhMe	96	40 (*R*)
10		DCM	50	49 (*R*)
11	(*S*,*S*,*S*,*S*)-Dp*b*BINOL (**4e**)	PhMe	66	70 (*S*)
12		DCM	16	60 (*S*)
13	(*R*,*R*)-Pr*bH*$_8$BINOL (**7**)	PhMe	97	81 (*R*)
14		DCM	62	80 (*R*)
15	(*S*,*S*,*S*,*S*)-Dp*bH*$_8$BINOL (**12**)	PhMe	55	62 (*S*)
16	—	PhMe	75	—

[a] Reaction conditions: 0.25 mmol of PhCHO, 0.05 mmol of ligand, 0.75 mmol of Et_2Zn and 0.4 mmol of $Ti(O^iPr)_4$ in 2 mL of solvent; T=0 °C.
[b] Conversion after 5 h reaction.

(*R*,*R*)-Bu*b*BINOL **4c**, a ligand that also contains four carbon atoms between the two hydroxynaphthyl units. (Table 1, entry 5–6 and 7–10).

Contrarily, when (*S*,*S*,*S*,*S*)-Dp*b*BINOL **4e** was used as ligand, a significant increase in the enantioselectivity (70% in the (*S*) product) was obtained with a concomitant decrease of the catalytic activity (Table 1, entry 11 and 12). These results indicate a matching/mismatching effect between the chirality of the BINOL and that of the link fragment.

In order to evaluate the effect of the presence of two units of H_8BINOL in the ligands that gave catalytic species with higher enantiodiscrimination we enlarged these studies using as ligands (*R*,*R*)-Pr*bH*$_8$BINOL **7** and (*S*,*S*,*S*,*S*)-Dp*bH*$_8$BINOL **12** (Table 1, entries 11–14). In both solvents, the catalyst with (*R*,*R*)-Pr*b*H$_8$BINOL **7** yielded a significant improvement in the stereoselectivity (ca. 80%) of the reaction when compared with (*R*,*R*)-PrbBINOL (Table 1, entry 3,4 and 13–14). However, it should be noted that with (*R*,*R*)-Pr*b*H$_8$BINOL a significant influence of the solvent in the catalytic activity was observed, being the highest activity obtained in toluene.

Surprisingly the use of (*S*,*S*,*S*,*S*)-Dp*bH*$_8$BINOL **12** did not give the expected enhancement in the enantioselectivily of the process when compared with the non-reduced parent.(Table 1, entry 11, 15).

The overall results are indicative that a cooperative effect between the structure of the BINOL unit and the size and structure of the di-ether bridge is crucial for the achievement of optimal enantiodiscrimination. It should also be noticed that a competition from the background reaction was observed (Table 1, entry 16), which can contribute to lowering the ee of some of the less active catalytic processes.

Additionally, recently we obtained spectroscopic and computational support that the involvement of chelate titanium complexes is fundamental for the achievement of high enantioselective catalytically active species, being the ee strongly dependent from the Ti/ligand molar ratio reaching a maximum at ca. 8.[35]

3. Conclusion

In summary, this paper describes several versatile synthetic approaches for the synthesis of a library of new chiral bis-BINOL-2,2′-ethers, containing different bridging linkages between the two BINOL or H_8BINOL. Monoprotection of BINOL followed by coupling with the desired ditosyl derivative, and subsequent hydroxyl deprotection using BBr_3, at low temperature, allows the preparation of bis-BINOL-2,2′-ethers with alkyl ether bridges with high overall yield. Furthermore, when hydrogenolysis, over Pd/C, was used as synthetic strategy for the benzyl deprotection, at moderate H_2 pressure, a concomitant partial aromatic naphthyl hydrogenation was obtained allowing the preparation of 7 with high yield.

By other side, when the ether bridge contains a benzylic fragment, the coupling of the BINOL-tin acetal with the diiodo-*o*-xylene revealed to be another versatile alternative. So, the synthetic strategies herein reported easily allow the enlargement of this library.

The $Ti(O^iPr)_4$ complexes of these ligands showed high activity in the catalytic ethylation of aromatic aldehydes. However, the size and structure of the bridge in the ligand has revealed to be critical with regard to the stereoselectivity of the catalytic reaction, being the ligands Pr*b*BINOL, (*S*,*S*,*S*,*S*)-Dp*b*BINOL and Pr*b*H$_8$BINOL the ones that show better enantioselectivity in the secondary alcohol obtained (ee ca. 80%). The results also indicate an appreciable interaction between the stereogenic centers on the link fragment and the axial chirality of the binaphthyl fragments, since diastereoisomeric ligands 3d and 3e not only yield opposite configurations of 1-phenylpropan-1-ol, but also produce significant differences in the ee achieved.

4. Experimental

4.1. General information

All catalytic and synthetic reactions were performed using standard Schlenk techniques, under N_2 inert atmosphere. Glassware was oven-dried. Solvents were purified by standard procedure and reagents were used as received. Thin-layer chromatography (TLC) was performed on Merck silica gel 60 TLC-plates P_{254}. Flash chromatography was carried out on silica gel (Aldrich, 220–440 mesh). ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ solution on Bruker 250, 300 or 400 spectrometers. High resolution ESI mass spectrometer Bruker microTOFQ was used to characterize the new ligands. For the catalytic reactions, conversion and chemoselectivity were obtained by gas chromatography on an Agilent-6890, equipped with a capillary HP5 column (30 m×0.32 mm i.d., 0.25 μm film thickness, carrier gas N_2, F.I.D. detector). The enantiomeric excesses and absolute configuration were measured with Konik-300C gas chromatograph equipped with β-cyclodextrin capillary column (Supelco β-Dex120, 30 m×0.25 mm) against optically pure (*R*) and (*S*)-2-phenyl-2-propanol. Uncorrected melting points were recorded on an Electrothermal capillary melting point apparatus.

4.2. Ligand synthesis

4.2.1. (R)-2′-(Benzyloxy)-1,1′-binaphthyl-2-ol (R)-BnBINOL ***1***. The compound was synthesized by slightly modifications of Mitsunobu reaction. To a stirred solution of (*R*)-binaphthol (5 g, 17.5 mmol), PPh_3 (4.59 g, 17.5 mmol) and benzyl alcohol (2.1 mL, 20 mmol), in dry THF (200 mL), a solution of diethyl azodicarboxylate (DEAD) (7.7 mL, 40% in toluene, 17.5 mmol) was added dropwise. The reaction was kept with stirring at room temperature, during 48 h. Then, the mixture was evaporated under reduced pressure. The residue was redissolved in dichloromethane and washed with water and brine. After partial evaporation of the solvent at reduced pressure, the residue was purified by silica gel column chromatography using CH_2Cl_2: *n*-hexane (1:1) as eluent. After evaporation of the solvent, the solid was recrystallized from toluene/*n*-hexane,

to afford (**2**) as a white solid, yielding 5.73 g (87%). The physical and spectroscopic data is in agreement with the literature.[26]

*4.2.2. General procedure for the synthesis of ditosylalkanes **2a–c**.* To a water solution (50 mL) of sodium hydroxide (10.5 g, 265 mmol) the desired diol (75 mmol) dissolved in THF (50 mL) was added. The reaction mixture was maintained, with stirring, at 0 °C and a solution of *p*-toluenesulfonyl chloride (31.5 g, 665 mmol) in THF (75 mL) was added dropwise (2 h). The reaction was stirred at 0 °C during another 2 h. The mixture was then poured into an aqueous solution of hydrochloric acid (10%) at 0 °C. The precipitated ditosylalkanes were filtered, washed with water and also with an aqueous solution of sodium hydrogen carbonate. The white solid was dried under vacuum. Recrystallization from AcOEt/MeOH gave the desired ditosylalkane. Yield of **2a** 23.89 g (86%); **2b** 26.79 g (93%); **2c** 17.93 g (60%). Physical and spectroscopic data are in agreement with those previously reported.[36]

*4.2.3. Synthesis of [(4S,5S)-2,2-dimethyl-1,3-dioxolane-4,5-diyl]bis-(methylene) bis(4-methylbenzenesulfonate) **2d**.* This product was prepared from diethyl tartrate as previously described, yielding 53%. Spectroscopic data were in agreement those previously reported.[32]

*4.2.4. General procedure for the synthesis of 2,2′-bis-BINOLate ethers **3a–d**.* To a suspension of sodium hydride (160 mg, 60% in paraffin, 4 mmol), in dry dimethylformamide (DMF) (10 mL, 0 °C), a solution of **1** (2.7 mmol), in dry DMF (5 mL), was dropwise added (30 min.). A solution of the desired ditosylalkane (**2a–d**) (1.3 mmol) in dry DMF was then slowly to the previous mixture (0 °C, 1 h). After the addition of ditosylalkane was completed, the reaction was stirred along 6 h at 80 °C. After cooling, water was added dropwise (0 °C) and the organic compound was extracted with CH_2Cl_2. The organic layer was washed with water and brine solution, and the concentrated organic phase was purified by flash chromatography using CH_2Cl_2/*n*hexane (2:1) as eluent. The 2,2′-bis-BINOLate ethers **3a–d** were separated from the excess of (*R*)-2′- (benzyloxy)-1,1′-binaphthyl-2-ol. Finally, the crudes were recrystallized from AcOEt/Pr^{i}OH, yielding the 2,2′-bis-BINOLate ethers **3a–d** as white powders.

*4.2.4.1. 1,2-Bis[(R)-2′-(benzyloxy)-1,1′-binaphthyl-2-yloxy]ethane **3a**.* Yield 720 mg (71%); ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.82 (dd, *J*=7.8 Hz, 4H), 7.62 (d, *J*=9.4 Hz, 2H), 7.33–7.03 (m, 22H), 6.90 (d, *J*=8.8 Hz, 2H), 6.84 (d, *J*=6.4 Hz, 4H), 4.88 (s, 4H), 3.85 (s, 4H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ=153.39, 153.00, 136.45, 133.05, 132.67, 128.45, 128.40, 128.26, 128.16, 127.03, 126.60, 126.23, 125.80, 125.20, 125.10, 124.45, 122.67, 122.62, 119.72, 119.49, 115.33, 115.05, 70.12, 67.96 ppm. Mp 85–86 °C. MS (ESI): *m*/*z*=801.2960 (M^+Na), calcd. For $C_{56}H_{42}O_4Na^+$ 801.2975.

*4.2.4.2. 1,3-Bis[(R)-2′-(benzyloxy)-1,1′-binaphthyl-2-yloxy]-propane **3b**.* Yield 876 mg (85%); ^{1}H NMR (250 MHz, $CDCl_3$,): δ=7.92–7.85 (m, 8H), 7.35–6.85 (m, 26H), 4.95 (s, 4H), 3.60 (m, 4H), 1.53 (m, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ=154.17, 154.12, 137.73, 134.21, 129.61, 129.3, 128.26, 128.01, 127.45, 127.02, 126.43, 126.32, 125.74, 125.60, 125.50, 123.92, 123.60, 122.91, 119.88, 116.31, 65.48, 29.40 ppm. Mp 80–82 °C; (ESI): *m*/*z*=815.3109 (M^+Na), calcd for $C_{57}H_{44}O_4Na^+$ 815.3132.

*4.2.4.3. 1,4-Bis[(R)-2′-(benzyloxy)-1,1′-binaphthyl-2-yloxy]-butane **3c**.* Yield 976 mg (93%); ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.80–7.73 (m, 8H), 7.27–6.99 (m, 20H), 6.97–6.75 (m, 6H), 4.82 (s, 4H), 3.54–3.48 (m, 2H), 3.42–3.35 (m, 2H), 1.41 (m, 4H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ=154.33, 154.00, 137.55, 134.13, 134.09, 129.35, 129.20, 129.14, 128.04, 127.82, 127.22, 126.69, 126.11, 125.80,125.49, 125.45, 123.60, 123.45, 120.93, 120.10, 116.03, 115.50, 71.06, 68.30, 25.06 ppm. Mp 74–75 °C; MS (ESI): *m*/*z*=829.3285 (M^+Na), calcd for $C_{58}H_{46}O_4Na^+$ 829.3288.

*4.2.4.4. (4S,5S)-4,5-Bis(((R)-2′-(benzyloxy)-1,1′-binaphthyl-2-yl-oxy)methyl)-2,2-dimethyl-1,3-dioxolane **3d**.* Yield 857 mg (75%); ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.91 (d, *J*=12 Hz, 2H), 7.88 (d, *J*=8 Hz, 2H), 7.80 (d, *J*=12 Hz, 2H), 7.77 (d, *J*=8 Hz, 2H), 7.35–7.03 (m, 20H), 6.96 (d, *J*=12 Hz, 2H), 4.25 (d, *J*=4 Hz, 4H), 4.91 (s, 4H), 3.49 (m, 2H), 3.15 (m, 4H), 1.26 (s, 6H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ=154.08, 153.79, 137.47, 133.98, 129.38, 129.34, 129.23, 128.10, 127.89, 127.84, 127.28, 126.72, 126.32, 126.28, 125.45, 125.37, 123.69, 120.75, 120.00, 116.09, 115.13, 108.80, 75.30, 71.24, 68.12, 29.71, 26.06 ppm. Mp 150–151 °C. MS (ESI): *m*/*z*=901.3479 (M^+Na), calcd for $C_{61}H_{50}O_6Na^+$ 901.3500.

*4.2.4.5. (4S,5S)-4,5-Bis(((S)-2′-(benzyloxy)-1,1′-binaphthyl-2-yloxy)-methyl)-2,2-dimethyl-1,3-dioxolane **3e**.* Yield 742 mg (65%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (t, *J*=8.5 Hz, 4H), 7.79 (dd, *J*=14.1, 8.6 Hz, 4H), 7.42–7.00 (m, 20H), 6.95 (d, *J*=8.4 Hz, 2H), 6.85 (d, *J*=6.0 Hz, 4H), 4.91 (s, 4H), 3.49 (m, 2H), 3.27–3.06 (m, 4H), 1.54 (s, 6H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 154.08, 153.79, 137.47, 133.98, 129.38, 129.34, 129.23, 128.10, 127.89, 127.84, 127.28, 126.72, 126.32, 126.28, 125.45, 125.37, 123.69, 120.75, 120.00, 116.09, 115.13, 108.80, 75.30, 71.24, 68.12, 29.71, 26.06. Mp 150–151 °C. MS (ESI): *m*/*z*=901.3479 (M^+Na), calcd for $C_{61}H_{50}O_6Na^+$ 901.3500.

4.2.5. General procedure for the synthesis of bis-BINOL-2,2′-ethers.

*4.2.5.1. Via Pd/C hydrogenolysis (**4a–e**).* A solution of the desired 2,2′-bis-BINOLate ethers **3a–e** (1.88 mmol) in AcOEt/Pr^{i}OH (3:1) in the presence of Pd/C 5% was hydrogenated in a Parr apparatus at 3 bar for 48 h at room temperature. The reaction mixture was filtrated in Celite, and the residue washed with methanol. After evaporation of the solvent the desired bis-BINOL-2,2′-ether was recrystallized from toluene/*n*-hexane. Yield of (**4a**) 483.4 mg (42%); (**4b**) 494.5 mg (58%); (**4c**) 746.3 mg (62%); physical and spectroscopic data are coherent with those previously described.[22]

*4.2.5.1.1. (1R,1″R)-2′,2″-((4S,5S)-2,2-Dimethyl-1,3-dioxolane-4,5-diyl)-bis(methylene)bis(oxy)di-1,1′-binaphthyl-2-ol **4d**.* Yield 853.9 mg (65%): ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.68 (d, *J*=8 Hz, 2H), 7.76 (d, *J*=8 Hz, 2H), 7.94 (d, *J*=8 Hz, 2H), 7.33–7.09 (m, 16H), 6.92 (t, *J*=8 Hz, 2H), 4.76 (br s, 2H), 3.61 (m, 2H), 3.15 (m, 4H), 2.22 (s, 6H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ=153.80, 150.19, 129.87,128.78, 128.62, 128.01, 127.96, 127.20, 127.06,126.31, 125.38, 123.81, 123.61, 123.42, 122.10, 116.74, 116.50, 114.94, 114.10, 113.93, 73.98, 66.93, 28.34 ppm. Mp 89–91 °C. (ESI): *m*/*z*=697.2581(M^-), calcd for $C_{47}H_{37}O_6^-$ 697.2585.

*4.2.5.1.2. (1S,1″S)-2′,2″-((4S,5S)-2,2-Dimethyl-1,3-dioxolane-4,5-diyl)-bis(methylene)bis(oxy)di-1,1′-binaphthyl-2-ol **4e**.* Yield 841 mg (64%): ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.70 (d, *J*=8 Hz, 2H), 7.76 (d, *J*=8 Hz, 2H), 7.94 (d, *J*=8 Hz, 2H), 7.09–7.33 (m, 16H), 6.93 (t, *J*=8 Hz, 2H), 4.75 (br s, 2H), 3.61 (m, 2H), 3.15 (m, 4H), 2.22 (s, 6H), ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ=153.80, 150.19, 129.87, 128.78, 128.60, 128.00, 127.95, 127.20, 127.10, 126.31, 125.38, 123.81, 123.61, 123.42, 122.10, 116.74, 116.50, 114.94, 114.10, 113.93, 73.98, 66.93, 28.34. (ESI): *m*/*z*=697.2583(M^-), calcd for $C_{47}H_{37}O_6^-$ 697.2585.

*4.2.5.2. Via BBr **4a–c**.* A BBr_3 solution (1 M in CH_2Cl_2, 3.1 mL), was added to a dry CH_2Cl_2 solution, of the desired **3a–c** (20 mL, 1.88 mmol) and the reaction was kept, with stirring, along 2 h maintaining the temperature at −78 °C. The reaction mixture was extracted with dichloromethane, and then washed with HCl solution (2 N). The organic phase was dried over $MgSO_4$ and the concentrated crude was purified by flash chromatography using CH_2Cl_2 as eluent. The compound was recrystallized from toluene/*n*-hexane. The bis-BINOL-2,2′-ethers were obtained as a white powder. Yield of **4a** 921 mg (80%), **4b** 918 mg (78%), **4c** 987 mg (82%).

Physical and spectroscopic data were in agreement with those previously described.[22]

4.2.6. Synthesis of (1R,1″R)-2′,2″-(propane-1,3- diylbis(oxy))bis-(5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl-2-ol) ***7***. A solution of **3b** (1.88 mmol) in $CHCl_3$/MeOH (3:1) in the presence of Pd/C 5% was submitted to 35 bar of H_2 along 72 h at the temperature of 35 °C. The reaction mixture was filtrated in Celite, and the residue was washed with methanol. Then, the mixture was evaporated under reduced pressure and the residue was purified by silica gel column chromatography using dichloromethane as eluent. The desired fraction was evaporated yielding (1*R*,1″*R*)-2′,2″-(propane-1,3-diylbis(oxy))bis(5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl-2-ol) as a white powder. Yield 945.78 mg (80%); ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.08 (d, *J*=8.3 Hz, 2H (H_4)), 6.99 (d, *J*=8.3 Hz, 2H, ($H_{4'}$)), 6.71 (d, *J*=8.3 Hz, 2H, (H_2)), 6.63 (d, *J*=8.3 Hz, 2H, ($H_{2'}$)), 4.37 (br s, 2H, (O*H*)), 3.80–3.66 (m, 4H,(O*CH*$_2$)), 2.81–2.73- (m, 8H, ($H_{8,8'}$)), 2.36–2.02 (m, 8H,, ($H_{5,5'}$)), 1.83–1.34 (m, 18H, ($H_{6,6',7,7'}$*CH*$_2$)) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): 154.92(C_2), 150.45($C_{2'}$), 138.19(Ar_q), 136.46(Ar_q), 130.71(Ar_q), 130.54(Ar–*C*H), 129.44(Ar–*C*H), 129.19 (Ar_q), 123.35 (Ar_q–*Ar*$_q$), 122.81(Ar_q–*Ar*$_q$), 113.09 (Ar–*C*H), 110.67 (Ar–*C*H), 64.74 (O*C*H$_2$), 29.72 (*C*H$_2$), 29.22 (*C*H$_2$), 27.57 (*C*H$_2$), 27.43 (*C*H$_2$), 23.58 (*C*H$_2$), 23.49 (*C*H$_2$), 23.43 (*C*H$_2$), ppm. MS (ESI): *m*/*z*=651.3442 (M^+Na), calcd. For $C_{43}H_{48}O_4Na^+$ 651.3445.

4.2.7. Tin acetal procedure.

4.2.7.1. (R)-4,4-Dibutyldinaphtho[2,1–d:1′,2′f][1,3,2]-dioxostannepine ***5***. A round bottomed flask fitted with a Dean–Stark head was charged with (*R*)-binaphthol (5 g, 1.75 mmol) and dibutyltin oxide (4.3 g, 1.75 mmol) in 1,2-dichloroethane (100 mL), the mixture was refluxed, under argon, with intermittent removal of water azeotrope. The evolution of the reaction was carried following the disappearance of the hydroxyl vibrational IR signal (3500 cm^{-1}) of binaphthol (ca. 4 h). The solvent was then removed under reduced pressure giving a quantitative yield of product, which was used without further purification. The physical and spectroscopic data are in good agreement with those previously reported in the lit.[33]

4.2.7.2. Synthesis of (R,R)-α,α′-bis[2′(2-hydroxy-1,1′-binaphthyl)Oxy]-o-xylene ***6***. 1,2-Bis-(iodomethyl)-benzene, prepared by reaction de dibromo derivative with NaI in acetone, (3 g, 8.22 mmol) dissolved in dry toluene, was added to a toluene solution of **5** (6.69 g, 13.7 mmol) (50 mL toluene) under inert atmosphere. The reaction was kept at the temperature of 120 °C during 72 h.

After cooling to room temperature, the mixture was treated with a solution of HCl in dioxane (1.7 M) and then the solvent was evaporated under reduced pressure. The crude was extracted with in ethyl acetate and separated from the salts by filtration. The solution was washed with water and brine and the resulting organic phase was dried over $MgSO_4$. The mixture was purified by flash chromatography using CH_2Cl_2: *n*-hexane (3:1) as eluent. The crude was recrystallized from toluene/*n*-hexane, yielding the desired (*R*,*R*)-α,α′-bis{2′(2-hydroxy-1,1′-binaphthyl)oxy}-*o*-xylene **7** as a white powder. Yield 1.85 g (40%); ^{1}H NMR (300 MHz, $CDCl_3$): 7.90 (t, *J*=9.0 Hz, 4H), 7.80 (t, *J*=9.0 Hz, 4H), 7.37 (d, *J*=8.0 Hz, 2H), 7.26–7.13 (m, 12H), 6.95–6.89 (m, 6H), 5.30 (br s, 2H), 4,75 (m, 4H) ppm. ^{13}C NMR (101 MHz, CDCl3): δ=154.53, 151.07, 134.60, 133.81, 133.65, 130.72, 129.66, 129.47, 128.89, 128.29,127.97, 127.69, 127.10, 126.30, 124.85, 124.67, 124.26, 123.03, 117.28, 116.33, 115.65, 114.89, 68.83 ppm. Mp 92–93 °C. (ESI): *m*/*z*=697.2356 (M^+Na), calcd for $C_{48}H_{34}O_4Na^+$ 697.2349.

4.2.8. (S)-2′-(Benzyloxy)- 5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl-2-ol (S)-BnH$_8$*BINOL* ***9***. The compound was synthesized by slightly modifications of Mitsunobu reaction.[26] To a stirred solution of (*S*)-H_8BINOL (5.2 g, 17.5 mmol), PPh_3 (4.59 g, 17.5 mmol), and benzyl alcohol (2.1 mL, 20 mmol), in dry THF (200 mL), a solution of diethyl azodicarboxylate (DEAD) (7.7 mL, 40% in toluene, 17.5 mmol) was added dropwise. The reaction was kept with stirring at room temperature, during 48 h. Then, the mixture was evaporated under reduced pressure. The residue was redissolved in dichloromethane and washed with water and brine. After partial evaporation of the solvent at reduced pressure, the residue was purified by silica gel column chromatography using CH_2Cl_2: *n*-hexane (1:1) as eluent,and two fraction were collected. After evaporation of the solvent of fraction 1, the solid was recrystallized from toluene/*n*-hexane, to afford **9** as a white solid, yielding 5.4 g (80%) of (*S*)-2′-(benzyloxy)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl-2-ol (*S*)-BnH$_8$BINOL (9): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.10 (m, 5H), 7.03 (dd, J^3=13.5 Hz, J^3=8.4 Hz, 2H), 6.80 (dd, J^3=8.3 Hz, J^3=3.5 Hz, 2H), 4.99 (s, 2H), 4.39 (bs, 1H), 2.76 (dd, J^1=13.8 Hz, J^3=6.5 Hz, 4H), 2.41–2.03 (m, 4H), 1.80–1.52 (m, 8H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 154.38, 150.18, 138.19, 137.66, 136.13, 130.90, 130.17, 129.35, 129.09, 128.33, 127.38, 126.54, 123.03, 122.80, 112.12, 111.28, 70.04, 29.38, 29.32, 27.36, 27.08, 23.22, 23.18, 23.07, 22.98 ppm. Mp 101–102 °C. MS (ESI): *m*/*z*=407.1982 (M^+Na), calcd for $C_{27}H_{28}O_2Na^+$ 407.1982.

After evaporation of the solvent of fraction 2, the solid was recrystallized from toluene/*n*-hexane, to afford 10 as a white solid, yielding 683 mg (10%) of (*S*)-2,2′-bis(benzyloxy)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl (10): ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.09–7.03 (m, 6H), 7.02–6.95 (m, 4H), 6.91 (d, *J*=8.4, 2H), 6.66 (d, *J*=8.3, 2H), 4.86 (s, 4H), 2.67 (t, *J*=5.7, 4H), 2,33–2.07 (m, 4H), 1.68–1.48 (m, 8H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 152.60, 137.12, 135.85, 127.50, 127.17, 127.08, 126.95, 126.00, 125.84, 125.64, 125.36, 109.90, 69.14, 28.45, 26.27, 22.23, 22.16 ppm. Mp 58–61 °C. MS (ESI): *m*/*z*=497.2441 (M^+Na), calcd for $C_{34}H_{34}O_2Na^+$ 497.2451.

4.2.9. (4S,5S)-4,5-Bis(((S)-2′-(benzyloxy)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl-2-yloxy)methyl)-2,2-dimethyl-1,3-dioxolane ***11***. To a suspension of sodium hydride (160 mg, 60% in paraffin, 4 mmol), in dry dimethylformamide (DMF) (10 mL, 0 °C), a solution of **9** (2.7 mmol), in dry DMF (5 mL), was added dropwise (30 min.). A solution of the desired ditosylalkane **2d** (1.3 mmol) in dry DMF was then slowly added to the previous mixture at 0 °C during 1 h. After total addition of the desired ditosylalkane the reaction was stirred along 6 h at 80 °C. After cooling, water was added dropwise (0 °C) and the organic compound was extracted with CH_2Cl_2. The organic layer was washed with water and brine solution, and the concentrated organic phase was purified by flash chromatography using CH_2Cl_2/*n*hexane (2:1) as eluent, yielding 743 mg of **11** (65%) after evaporation of the solvent and recrystallized from AcOEt/Pr^{i}OH. (4*S*,5*S*)-4,5-bis(((*S*)-2′-(benzyloxy)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl-2-yloxy)methyl)-2,2-dimethyl-1,3-dioxolane (**11**): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20–7.04 (m, 6H), 6.98 (dd, J^3=17.8, J^3=8.1 Hz, 8H), 6.67 (d, *J*=8.3 Hz, 2H), 6.54 (d, *J*=8.4 Hz, 2H), 4.74 (s, 4H), 3.80 (m, 2H), 3.72–3.38 (m, 4H), 2.86–2.60 (m, 8H), 2.42–2.18 (m, 4H), 2.18–2.00 (m, 4H), 1.78–1.48 (m, 16H), 0.97 (s, 6H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 153.66, 153.55, 138.16, 136.73, 136.63, 129.96, 129.93, 128.51, 128.40, 128.10, 127.01, 126.68, 126.29, 126.23, 110.97, 110.04, 109.30, 75.58, 70.09, 67.19, 29.47, 29.41, 27.23, 27.18, 26.33, 23.24, 23.20, 23.14 ppm. 75–77 °C. MS (ESI): *m*/*z*=917.4748 (M^+Na), calcd for $C_{61}H_{66}O_6Na^+$ 917.4752.

4.2.10. (1′S,1′S)-2′,2″-((4S,5S)-2,2-Dimethyl-1,3-dioxolane-4,5 diyl)-bis(methylene)bis(oxy)bis(5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-bibenzobenzen-2-ol) ***12***. A solution of **11** (1.88 mmol) in AcOEt/Pr^{i}OH (3:1) in the presence of Pd/C 5% was hydrogenated in a Parr apparatus at 3 bar for 48 h at room temperature. The reaction mixture was filtrated in Celite, and the residue was washed with methanol. After evaporation of the solvent and recrystallized from toluene/

n-hexane the desire product was isolated, yield 912 mg (68%) ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 (d, J=6.6 Hz, 2H), 7.17 (d, J=7.4 Hz, 2H), 7.09 (d, J=8.4 Hz, 2H), 6.97 (d, J=8.3 Hz, 2H), 4.45 (br s, 2H), 3.87–3.68 (m, 4H), 3.53 (m, 2H), 2.84–2.63 (m, 8H), 2.35 (s, 6H), 2.30–2.01 (m, 8H), 1.83–1.61 (m, 16H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 153.99, 149.86, 137.97, 136.02, 131.33, 130.32, 129.51, 129.37, 129.04, 128.23, 125.30, 122.84, 122.48, 112.29, 110.83, 70.27, 69.35, 30.91, 29.28, 27.26, 27.04, 23.13, 22.98, 22.94, 21.45 ppm. Mp 81–82 °C. MS (ESI): m/z=737.3800, calcd for 737.3813 $C_{47}H_{54}O_6Na^+$.

5. General procedure for the catalytic reactions

Titanium isopropoxide (121 μL, 0.4 mmol) was added via syringe to the desired bis-BINOL-2,2′-ethers (0.05 mmol) in the appropriate freshly dried solvent (2 mL), under N_2 atmosphere (15 min). To the resulting yellow solution diethylzinc (0.75 mL, 1.0 M in hexane, 0.75 mmol) was added, followed by the addition of arylic aldehyde (0.25 mmol). The reaction was kept at the appropriate temperature for 5 h and quenched with 2 N HCl. The aqueous layer was extracted with ethyl acetate and evaporated. The solid was redissolved in pentane. The ligand precipitates and was removed by filtration. The resulting solution was analyzed by GC, GC/MS and GC equipped with chiral column.

Acknowledgements

The authors thank financial support from Portuguese FCT through project PTDC/QUI/66015/2006, Merquinsa (Barcelona, Spain), and the Spanish DGI through project BIO2006-14420-CO2-02. ARA also thanks FCT for a PhD grant (SFRH/BD/21314/2005).

References and notes

1. Rosini, C.; Franzini, L.; Raffaelli, A.; Salvadori, P. *Synthesis* **1992**, 503–517.
2. Pu, L. *Chem. Rev.* **1998**, *98*, 2405–2494.
3. Baeza, A.; Casas, J.; Nájera, C.; Sansano, J. M.; Saá, J. M. *Angew. Chem., Int. Ed.* **2003**, *42*, 3143–3146.
4. Qian, C.; Zhu, C.; Huang, T. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2131–2132.
5. Shibasaki, M.; Sasai, H.; Arai, T. *Angew. Chem., Int. Ed.* **1997**, *36*, 1236–1256.
6. Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H. *Comprehensive Asymmetric Catalysis*; Springer: Berlin, 1999; Vols. 1–3.
7. Chen, Y.; Yekta, S.; Yudin, A. K. *Chem. Rev.* **2003**, *103*, 3155–3211.
8. Brunel, J. M. *Chem. Rev.* **2007**, *107*, 1–45.
9. Nájera, C.; Sansano, J.; Saá, M. J. M. *Eur. J. Org. Chem.* **2009**, 2385–2400.
10. (a) Balsells, J.; Davis, T. J.; Carroll, P.; Walsh, P. J. *J. Am. Chem. Soc.* **2002**, *124*, 10336–10348; (b) Pescitelli, G.; Di Bari, L.; Salvadori, P. *Organometallics* **2004**, *23*, 4223–4229.
11. Cram, D. J.; Helgeson, R. C.; Peacock, S. C.; Kaplan, L. J.; Domeier, L. A.; Moreau, P.; Koga, K.; Mayer, J. M.; Chao, Y.; Siegel, M. G.; Hoffman, D. H.; Sogah, G. D. Y. *J. Org. Chem.* **1978**, *43*, 1930–1946.
12. Shen, X.; Guo, H.; Ding, K. *Tetrahedron: Asymmetry* **2000**, *11*, 4321–4327.
13. (a) Zhang, F.-Y.; Yip, C.-W.; Cao, R.; Chan, A. S. C. *Tetrahedron: Asymmetry* **1997**, *8*, 585–589; (b) Zhang, F.-Y.; Chan, A. S. C. *Tetrahedron: Asymmetry* **1997**, *8*, 3651–3655; (c) Reetz, M. T.; Merk, C.; Naberfeld, G.; Rudolph, J.; Gribenow, N.; Goddard, R. *Tetrahedron Lett.* **1997**, *38*, 5273–5276; (d) Chan, A. S. C.; Zhang, F.-Y.; Yip, C.-W. *J. Am. Chem. Soc.* **1997**, *119*, 4080–4081.
14. Waltz, K. M.; Carroll, P. J.; Walsh, P. J. *Organometallics* **2004**, *23*, 127–134.
15. Zhang, F.-Y.; Pai, C.-C.; Chan, A. S. C. *J. Am. Chem. Soc.* **1998**, *120*, 5808–5809.
16. Uemura, T.; Zhang, X.; Matsumura, K.; Sayo, N.; Kumobayashi, H.; Ohta, T.; Nozaki, K.; Takaya, H. *J. Org. Chem.* **1996**, *61*, 5510–5516.
17. Vogl, E. M.; Matsunaga, S.; Kanai, M.; Iida, T.; Shibasaki, M. *Tetrahedron Lett.* **1998**, *39*, 7917–7920.
18. Matsunaga, S.; Das, J.; Roels, J.; Vogl, E. M.; Yamamoto, N.; Iida, T.; Yamaguchi, K.; Shibasaki, M. *J. Am. Chem. Soc.* **2000**, *122*, 2252–2260.
19. Kumagai, N.; Matsunaga, S.; Kinoshita, T.; Harada, S.; Okada, S.; Sakamoto, S.; Yamaguchi, K.; Shibasaki, M. *J. Am. Chem. Soc.* **2003**, *125*, 2169–2178.
20. Asakawa, M.; Brown, C. L.; Pasini, D.; Stoddart, J. F.; Wyatt, P. G. *J. Org. Chem.* **1996**, *61*, 7234–7235.
21. Bähr, A.; Droz, A. S.; Püntener, M.; Neidlen, U.; Anderson, S.; Seiler, P.; Diederich, F. *Helv. Chim. Acta* **1998**, *81*, 1931–1963.
22. Jha, S. C.; Joshi, N. N. *Synth. Commun.* **2003**, *33*, 1005–1009.
23. Ojima, I. *Catalytic Asymmetric Synthesis*, 2nd ed.; Wiley-VCH: New York, NY, 2000.
24. (a) Wu, K.-H.; Gau, H.-M. *Organometallics* **2003**, *22*, 5193–5200; (b) Wu, K.-H.; Gau, H.-M. *Organometallics* **2004**, *23*, 580–588; (c) Hsieh, S.-H.; Gau, H.-M. *Chirality* **2006**, *18*, 569–574; (d) Walsh, P. J. *Acc. Chem. Res.* **2003**, *36*, 739–749.
25. Mitsunobu, O. *Synthesis* **1981**, 1–28.
26. (a) Takahashi, M.; Ogasawara, K. *Tetrahedron: Asymmetry* **1997**, *8*, 3125–3130; (b) Carrilho, R. M. B.; Abreu, A. R.; Petıcz, G.; Bayón, J. C.; Moreno, M. J. S. M.; Kollár, L.; Pereira, M. M. *Chem. Lett.* **2009**, *8*, 844–845.
27. David, S.; Hanessian, S. *Tetrahedron* **1985**, *41*, 643–663.
28. Green, J.; Woodward, S. *Synlett* **1995**, 155–156.
29. Martins, A. E.; Ford, T. M.; Bulkowski, J. E. *J. Org. Chem.* **1982**, *47*, 412–415.
30. Sugimura, T.; Yamada, H.; Inoue, S.; Tai, A. *Tetrahedron: Asymmetry* **1997**, *8*, 649–655.
31. Greene, T. W.; Wunts, P. G. M. *Protective Groups in Organic Synthesis*; Wiley: New York, NY, 1991; pp 14–87.
32. Kagan, H. B.; Dang-, T. P. *J. Am. Chem. Soc.* **1972**, *94*, 6429–6433.
33. Iwasaki, F.; Maki, T.; Onomura, O.; Nakashima, W.; Matsumura, Y. *J. Org. Chem.* **2000**, *65*, 996–1002.
34. Simas, A. B. C.; Pais, K. C.; Silva, A. A. T. *J. Org. Chem.* **2003**, *68*, 5426–5428.
35. Abreu, A. R.; Peral, D.; Pereira, M. M.; Rosado, M. T. S.; Eusébio, M. E. S.; Palacios, Ò; Bayon, J. C., submitted for publication.
36. Kyba, E. P.; Gokel, G. W.; De Jong, F.; Koga, K.; Sousa, L. R.; Siegel, M. G.; Kaplan, L.; Dotsevi, G.; Sogah, Y.; Cram, D. J. *J. Org. Chem.* **1977**, *42*, 4173–4184.