Modification of (1*R*,2*S*)-1,2-Diphenyl-2-aminoethanol for the Highly Enantioselective, Asymmetric Alkylation of *N*-Diphenylphosphinoyl Arylimines with Dialkylzinc

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Abstract: Experimental studies on the modification of (1*R*,2*S*)-1,2-diphenyl-2-aminoethanol, which is used to promote the alkylation of *N*-diphenylphosphinoyl benzalimine with diethylzinc, revealed that *N*-monosubstituted amino alcohols exhibited higher enantioselectivities than their *N*,*N*-disubstituted counterparts and imino alcohols. Application of the optimal chiral ligand **3c** to activate the reaction of *N*-diphenylphosphinoyl arylimines with diethylzinc and dibutylzinc resulted in excellent enantiomeric selectivities of up to 98% *ee*. The origin of the experimentally observed enantioselectivities was revealed by density functional calculations (B3LYP/6-31G*) on the transition structures of several model reactions.

Keywords: amino alcohols · asymmetric additions · density functional calculations · imines · zinc

Introduction

Chiral amines are widely used in the synthesis of natural products and physiologically active substances, in chiral separation, and in asymmetric synthesis as chiral auxiliaries.[1,2] There has been great interest in developing methods for asymmetric preparation of chiral amines.[3,4] Enantioselective nucleophilic addition of organometallic reagents to imines, which is very challenging, has been investigated in recent years.[4] Asymmetric alkylation of imines with dialkylzinc represents one of the most convenient routes to optically active amines. Since Soai and co-workers reported on the MOPEP (an ephedrine derivative)-mediated addition of diethylzinc to diphenylphosphinoylimine, enantioselective alkylations of *N*-diphenylphosphinoyl arylimines with dialkylzinc that employ chiral amino alcohols,[5a–f] chiral oxazolines,[5g–h] polymeric chiral amino alcohols,[5i–j] and chiral dendrimers[5k] as ligands have been described. A recent study in this area focused on the development of chiral complexes for a catalytic version of the reaction.[6] Many chiral amino alcohol ligands have been developed for the addition of diethylzinc to diphenylphosphinoylimines, but most of them are limited to the compounds containing a structurally rigid backbone.[5e,f] There is a trend in previous reports that structurally constrained chiral β-amino alcohols generally show much higher enantioselectivities than their structurally flexible counterparts.[5b–f] However, the synthesis of structurally rigid and restricted amino alcohols is inconvenient and often involves a multistep-synthesis.[5e,7] This makes the addition of diethylzinc to imines for the preparation of chiral amines too expensive to compete with other families of chiral ligands, especially if stoichiometric amounts are needed. Therefore, the development of easily accessible and economical chiral reagents is still worthwhile.

In our laboratory, metal complexes of chiral 1,2-diphenyl-2-aminoethanol and its derivatives have been developed with the aim of promoting several reactions that have exhibited high enantioselectivities in most cases.[8] Prompted by these results and the fact that the size of the substituent

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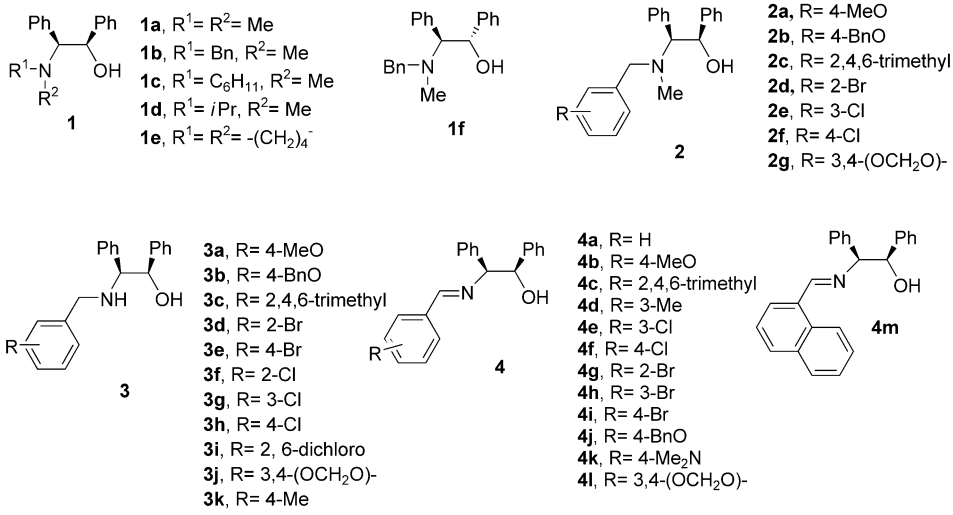
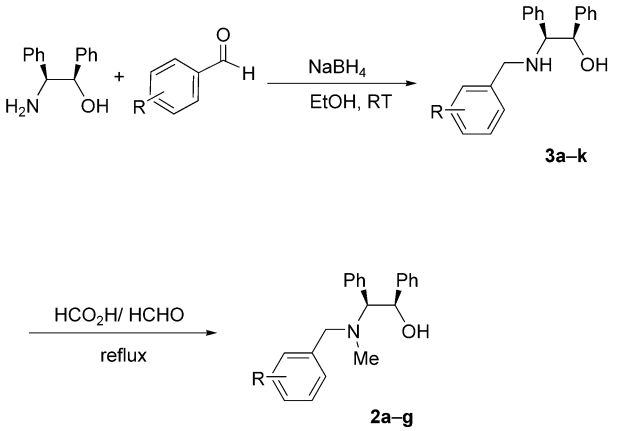
bonded to the nitrogen on chiral amino alcohols might play an important role in influencing enantioselectivity, we envisioned that highly enantioselective ligands for asymmetric diethylzinc addition to *N*-diphenylphosphinoylimines might be obtained by fine-tuning the substituents on the nitrogen center of chiral 1,2-diphenyl-2-aminoethanol. A preliminary report on this project has already been presented.[9] Herein we report the comprehensive investigation of a library of chiral β-amino alcohols (**1**–**4**), which exhibit subtle differences in their structures and which are derived from chiral 1,2-diphenyl-2-aminoethanol, for the asymmetric alkylation of imines with dialkylzinc. We also report a theoretical study that sheds light on the origin of the observed enantioselectivities (Scheme 1).



Scheme 1. Chiral ligands evaluated for this study.

Results and Discussion

Preparation of the chiral ligands: The preparation of *N*,*N*-disubstituted amino alcohols **1a**–**f** from chiral 1,2-diphenyl-2-aminoethanol has already been reported.[8] *N*,*N*-Disubstituted amino alcohols **2** bearing substituted phenyl and *N*-monosubstituted amino alcohols **3** were prepared according to a synthetic route shown in Scheme 2. The condensation of 1,2-diphenyl-2-aminoethanol with substituted benzaldehydes in anhydrous ethanol followed by reduction with $NaBH_4$ in one pot furnished **3a**–**k** with good-to-high yields. Compounds **3a**–**d**,**g**,**h**,**j** were treated with HCOOH and HCHO under refluxing conditions to provide **2a**–**g** in high yields.

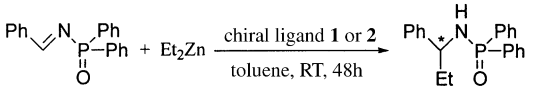


Scheme 2. The preparation of compounds **2** and **3**

Chiral imines **4a**–**m** were simply prepared by condensation of 1,2-diphenyl-2-aminoethanol with the corresponding aldehyde in the presence of anhydrous sodium sulfate. All these compounds were obtained as fine crystals, and were identified by NMR and IR spectra.

Asymmetric addition of diethylzinc to *N*-diphenylphosphinoyl benzalimine mediated by *N*,*N*-disubstituted amino alcohols 1 and 2: We systematically examined the effects of substituents on the enantioselectivity of the reaction of diethylzinc with *N*-diphenylphosphinoyl benzalimine as a standard substrate in the presence of stoichiometric amounts of *N*,*N*-disubstituted amino alcohols **1** or **2**. The size of the substituents bonded to the nitrogen atom in ligands **1** was important for achieving a high enantioselectivity in the reactions (Table 1). The ligand (1*R*,2*S*)-**1a**, which is excellent for enantioselective addition of diethylzinc to aldehydes,[8a] induced the reaction of **5a** with Et_2Zn in 89% *ee* (Table 1, entry 1). A slight improvement in the enantioselec-

Table 1. The addition of diethylzinc to *N*-diphenylphosphinoyl benzalimine **5a** in the presence of chiral *N*,*N*-disubstituted amino alcohols **1** or **2**.[a]



5a **6a**

Entry	Ligand	Yield [%][b]	*ee* [%][c]	Configuration[d]
1	**1a**	93	89	*R*
2	**1b**	90	94	*R*
3	**1c**	72	89	*R*
4	**1d**	91	85	*R*
5	**1e**	65	80	*R*
6	**1f**	92	40	*S*
7	**2a**	94	95	*R*
8	**2b**	63	92	*R*
9	**2c**	93	84	*R*
10	**2d**	35	91	*R*
11	**2e**	87	95	*R*
12	**2f**	94	93	*R*
13	**2g**	80	93	*R*

[a] The reaction was carried out at room temperature in the presence of stoichiometric amounts of amino alcohols for 48 h. [b] Yield of isolated product based on imine **5a**. [c] Determined by HPLC. [d] Determined by comparison of the retention time with the literature.

tivity was realized when the reaction was catalyzed by **1b**. A further increase in the steric hindrance of the substituents at the nitrogen atom in the chiral ligands led to a significant decrease in the enantioselectivity (Table 1, entries 3–5). Unlike the reported conformationally restricted amino alcohols,[5d–f] the use of the nitrogen-constrained ligand **1e** as a promoter resulted in a dramatic drop in both yield and enantioselectivity (Table 1, entry 5). This is possibly attributed to the rigidity of the pyrrolidine ring in the ligands which made it difficult for the ligand–zinc alkoxide system to coordinate to the substrate. Comparison of entries 2 and 6 in Table 1, clearly shows that the configuration of the product depends on the configuration of the carbon atom bonded to the hydroxy group on the ligands. When the configuration of this carbon atom was inverted while that of the carbon atom bonded to the nitrogen atom was retained, as shown from **1b** to **1f**, the configuration of the product was inverted from *R* to *S*. The ligand with the *erythro* form **1b** showed much better enantioselectivity than that with the *threo* form **1f**.

Most of the chiral *N*-methyl-*N*-aryl amino alcohols **2** gave good enantioselectivities with up to 95% *ee*. The aryl substituents in the ligands had a pronounced effect on the enantioselectivity. The ligands bearing a bulkier R group on the benzene ring hindered the enantioselectivity. Ligand **2a**, in which the R group was a 4-methoxy group, promoted the reaction to give the product **6a** in 94% yield with 95% *ee* (Table 1, entry 7), while **2b** containing a bulkier benzyloxy group resulted in a slightly reduced stereoselectivity of 92% *ee* (Table 1, entry 8). A further increase in the bulkiness of the R group by replacement of the 4-methoxybenzyl group in **2a** with a 2,4,6-trimethylbenzyl group to give **2c** led to a much lower *ee* of 84% (Table 1, entry 9). Most of the ligands bearing a halogen on a benzyl group provided excellent enantioselectivities. High enantioselectivities of 95% and 93% *ee* were obtained with **2e** (R = 3-Cl) and **2f** (R = 4-Cl), respectively (Table 1, entries 11 and 12). The ligand **2d** (R = 2-Br) also afforded a good enantioselectivity of 91% *ee*, but gave the product **6a** only in 35% yield (Table 1, entry 10).

Asymmetric addition of diethylzinc to *N*-diphenylphosphinoyl benzalimine mediated by *N*-monosubstituted amino alcohols 3: *N*,*N*-Disubstituted β-amino alcohols have been successfully employed for the addition of diethylzinc to carbonyl compounds with an extremely high enantioselectivity. Generally, an *N*,*N*-disubstituent on the amino alcohol was required to obtain high enantioselectivity.[10] Amongst the approximate 260 individual chiral amino alcohols recently reviewed by Pu and Yu for diethylzinc addition to aldehydes, only a few of the *N*-monosubstituted amino alcohols have given more than 90% *ee* in the addition of diethylzinc to aldehydes.[11] The use of *N*-monosubstituted β-amino alcohol to promote the addition of diethylzinc to diphenylphosphinoylimines with high enantioselectivities is also rare.[12] The dramatic dependence of enantioselectivity on the size of the *N*-substituent of the ligand **2** prompted us to screen the *N*-substituent with *N*-monosubstituted chiral amino alcohols **3**. It was encouraging that chiral amino alcohol **3a**, in which a methyl group was removed from the nitrogen atom as compared with its *N*,*N*-disubstituted analogue **2a**, provided an excellent enantioselectivity of 95% *ee*. This result indicated that *N*-monosubstituted β-amino alcohols could also serve as good ligands for the addition of diethylzinc to imine. Thus we surveyed other *N*-monosubstituted β-amino alcohols **3b–k** for their ability to promote the above-mentioned reaction. As shown in Table 2,

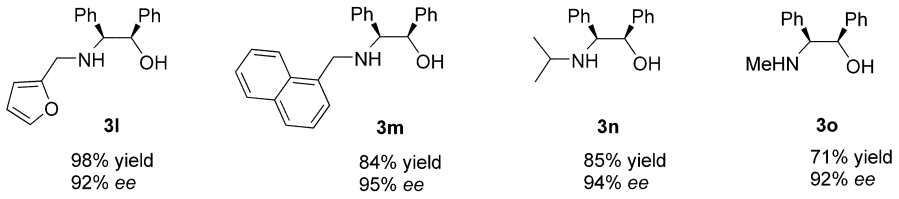
Table 2. The addition of diethylzinc to *N*-diphenylphosphinoyl benzalimine (**5a**) in the presence of the chiral amino alcohols **3**.[a]

Entry	Ligands	R	Yield [%][b]	*ee* [%][c]
1	**3a**	4-MeO	99	95
2	**3b**	4-BnO	68	95
3	**3c**	2,4,6-trimethyl	92	97
4	**3c**	2,4,6-trimethyl	81	93[d]
5	**3d**	2-Br	99	95
6	**3e**	4-Br	91	95
7	**3f**	2-Cl	90	94
8	**3g**	3-Cl	78	94
9	**3h**	4-Cl	99	94
10	**3i**	2,6-dichloro	91	96
11	**3j**	3,4-(OCH_2O)-	85	94
12	**3k**	4-Me	95	95

[a] The reaction was carried out at room temperature in the presence of stoichiometric amounts of amino alcohols for 48 h, unless specified otherwise. [b] Yield of isolated product based on imine **5a**. [c] Determined on HPLC, and the absolute configuration is *R*. [d] The reaction was promoted by 50 mol% of ligand **3c**.

all of the amino alcohols **3** afforded higher or similar enantioselectivities than the corresponding *N*,*N*-disubstituted compounds **2**. Ligands bearing a bulkier R group tended to induce a higher enantioselectivity, in contrast to the situation of *N*,*N*-disubstituted amino alcohols **2**. In particular, ligand **3c**, which contains a 2,4,6-trimethylbenzyl group, generated the highest enantioselectivity of 97% *ee* (Table 2, entry 3). However, ligand **2c** only resulted in 84% *ee* (Table 1, entry 9). If the R group is a halogen, as in ligands **3d–h**, the results also supported the tendency of a larger R group being beneficial to the enantioselectivity. For instance, ligand **3d**, which bears a Br on the benzyl group, gave an enantioselectivity of 95% *ee* (Table 2, entry 5), higher than those given by **3f–h** in which the R groups were Cl. However, the *N*,*N*-disubstituted amino alcohols **2d–f**, **2e**, and **2f** provided a higher stereochemical outcome than **2d**. The same substituent at a different position on the phenyl did not change the enantioselectivity. For instance, **3d**, which bears a 2-bromophenyl group, gave an identical enantioselectivity to **3e**, which bears a 4-bromophenyl group (Table 2, entries 5 and 6). Ligands **3f–h** also provided the same enantioselectivity of 94% *ee* for the reaction (Table 2, entries 7–9). Amino alcohol **3i**, with two chlorides positioned at C2 and C6 on the phenyl group promoted the reaction with 96% *ee* (Table 2, entry 10), which is higher than the amino alcohols (**3a**, **b**, **3d–h**, **3j**, and **3k**) that have a monosubstituted phenyl group. In the presence of 50 mol% of the best ligand **3c**, high yields of 81% and 93% *ee* were afforded (Table 2, entry 4).

N-monosubstituted β-amino alcohols **3l–o**, which bear other substituents, such as furyl, 2-naphthyl, isopropanyl, and a less sterically bulky methyl group, were also examined (Scheme 3). All these ligands afforded high enantioselectivities (92–95% *ee*) and high yields (71–98%). The results further indicate that the enantioselectivity is not very sensitive to the substituent on the nitrogen of the amino alcohol.



Scheme 3. Results observed with *N*-monosubstituted β-amino alcohols **3l–o**.

Asymmetric addition of diethylzinc to *N*-diphenylphosphinoyl benzalimine mediated by imino alcohols 4: In our recent work, we demonstrated that the chiral ligands incorporating sp^2-hybridized nitrogen with a hydroxy group promoted the addition of diethylzinc to imines with high enantioselectivity.[5g,h] Therefore, we believed that the imino alcohols should also be good chiral ligands for the reaction.

Chiral imino alcohols **4** were thus surveyed to promote the addition of diethylzinc to *N*-diphenylphosphinoyl benzalimine. As shown in Table 3, this family of chiral imino alcohols provided high enantioselectivities of up to 95% *ee* for the model reaction. Variation in the size of the substituent on the imino alcohols led to a slight change in the enantioselectivity. The best enantioselectivity was observed with the optimal ligand **4c** (Table 3, entry 3, 95% *ee*) and the lowest enantioselectivity was induced by ligand **4m** (Table 3, entry 13, 87% *ee*).

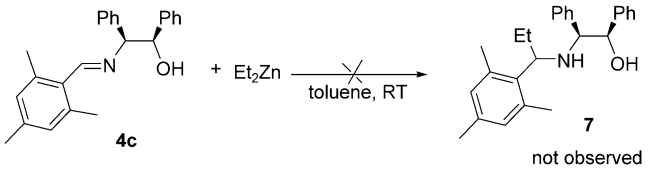
Table 3. The addition of diethylzinc to *N*-diphenylphosphinoyl benzalimine **5a** in the presence of the chiral imino alcohols **4**.[a]

Entry	Ligands	R	Yield[%][b]	*ee*[%][c]
1	**4a**	H	92	91
2	**4b**	4-MeO	85	92
3	**4c**	2,4,6-trimethyl	70	95
4	**4d**	3-Me	78	93
5	**4e**	3-Cl	74	92
6	**4f**	4-Cl	60	90
7	**4g**	2-Br	65	92
8	**4h**	3-Br	65	93
9	**4i**	4-Br	76	91
10	**4j**	4-BnO	56	90
11	**4k**	4-Me_2N	68	89
12	**4l**	3,4-(OCH_2O)-	60	91
13	**4m**	–	67	87

[a] The reaction was carried out at room temperature in the presence of stoichiometric amounts of amino alcohols for 48 h. [b] yield of isolated product based on imine. [c] Determined on HPLC, and the absolute configuration is *R*.

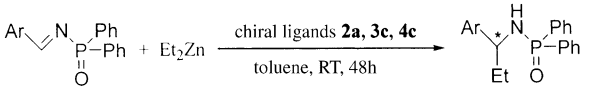
We found that the imino function of the ligands **4** was stable to diethylzinc. When the mixture of optical imino alcohol **4c** and three equivalents of diethylzinc was stirred at the room temperature for 48 h, compound **7** was not observed (Scheme 4).

Addition of diethylzinc to aromatic imines mediated by optimal ligands 2a, 3c, and 4c: After we finished the systematic investigation of the relationship between the ligand structure and the enantioselectivity, optimal ligands, **2a**, **3c**, and **4c** were extended to activate the addition of diethylzinc to other diphenylphosphinoylimines. The corresponding results are recorded in Table 4. In the presence of ligand **2a**, enantioselectivities of 94–96% were obtained for all of the imine substrates tested. Imino alcohol **4c** also promoted the reaction with high enantioselectivities of 94–96% *ee*, but with lower yield (70–81%) in comparison with its structural analogues **2a** (94–98%) and **3c** (86–97%). Basically, the substituents on the substrates had no



Scheme 4. The reaction of imino alcohol **4c** with three equivalents of diethylzinc.

Table 4. Asymmetric addition of diethylzinc to aromatic *N*-diphenylphosphinoyl imines **5a–e** promoted by **2a**, **3c**, and **4c**.[a]



5 **6**

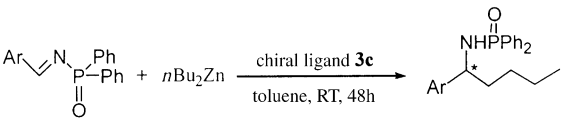
Ar	Imine	Ligand	Yield[%][b]	*ee*[%][c]
Ph	**5a**	**2a**	94	95
		3c	92	97
		3c	97	98[d]
		4c	70	95
4-$MeOC_6H_4$	**5b**	**2a**	82	95
		3c	89	97
		4c	73	94
3,4-(OCH_2O)-C_6H_3	**5c**	**2a**	90	95
		3c	92	97
		4c	70	95
4-MeC_6H_4	**5d**	**2a**	89	96
		3c	95	98
		4c	81	96
3-MeC_6H_4	**5e**	**2a**	98	94
		3c	86	96
		4c	62	94

[a] The reaction was carried out at room temperature in the presence of stoichiometric amounts of chiral ligands for 48 h. [b] Yield of isolated product based on imines. [c] Determined on HPLC. [d] The reaction was performed on the 1 mmol scale.

obvious effect on the enantioselectivity. Ligand **3c**, on average, gave a slightly higher enantioselectivity than ligands **2a** and **4c**. For all of the substrates examined, **3c** afforded enantioselectivities from 96% to 98% *ee*. Ligand **3c** not only gave the best results reported so far,[13] but it is also the most easily accessible. It is noteworthy that although stoichiometric amounts of amino alcohol had to be used, the chiral ligand could be easily recovered by flash chromatography.

Asymmetric addition of dibutylzinc to imines in the presence of ligand 3c: Asymmetric addition of butylmetallics to imines in the presence of chiral ligands has attracted great interest owing to chemical challenges and potential applications.[4b] Tomioka and co-workers were the first to report that the addition of butyllithium to *N*-arylimines in the presence of stoichiometric or substoichiometric amounts of amino ethers resulted in moderate-to-good enantioselectivities.[14] Itsuno and co-workers studied the addition of butyllithium to benzaldehyde *N*-(trimethylsilyl)imine in the presence of chiral promoters, such as alcohols, diols, and amino alcohols, to give the enantiomerically enriched primary amine with high yields and moderate *ee* values.[15] The use of both stoichiometric and catalytic amounts of (−)-sparteine in the addition of butyllithium to *N*-arylimines resulted in high yields and high enantioselectivities (<91% *ee*).[15b,16] In 1992, Soai et al. reported the use of a stoichiometric amount of (1*S*,2*R*)-MOPEP in the addition of dibutylzinc to *N*-diphenylphosphinoyl benzalimine (**5a**) with a moderate yield (56%) and a high enantioselectivity (87% *ee*).[5a] Since chiral ligand **3c** generally exhibited high enantioselectivity for the addition of diethylzinc to imines, we investigated the addition of dibutylzinc to *N*-diphenylphosphinoyl arylimines in the presence of ligand **3c**. As shown in Table 5, excellent

Table 5. The asymmetric addition of dibutylzinc to imines mediated by chiral amino alcohol **3c**.[a]

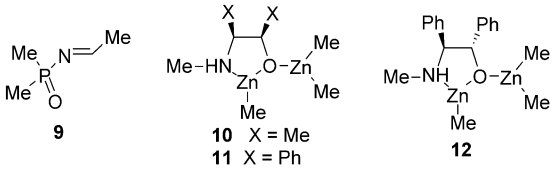


Ar	Imine	Yield [%][b]	*ee* [%][c]	Configuration[d]
Ph	**5a**	67	97	*R*
4-MeOC$_6$H$_4$	**5b**	50	95	*R*
3,4-(OCH$_2$O)-C$_6$H$_3$	**5c**	57	97	*R*
4-MeC$_6$H$_4$	**5d**	63	96	*R*
3-MeC$_6$H$_4$	**5e**	55	97	*R*
4-BrC$_6$H$_4$	**5f**	59	96	*R*

[a] The reaction was carried out in the presence of stoichiometric amounts of **3c**. [b] Yield of isolated product. [c] The *ee* values were determined on HPLC. [d] Determined by comparison of the retention time with the literatures.

enantioselectivities of 95–97% *ee* were observed. Compared with the addition of diethylzinc to imines, this reaction gave lower yields (50–67%). To the best of our knowledge, these results represent the highest enantioselectivities for the addition of a butylmetallic species to imines.

Theoretical modeling of the stereoselectivity: Theoretical calculations have been carried out to understand the origin of the observed enantioselectivities. Our study started with a simplified model. As shown in Scheme 5, the substrate was



Scheme 5. Models for the theoretical study

reduced to **9** and dimethylzinc was modeled instead of diethylzinc. Our model is similar to that used by Brandt et al. for the addition of diethylzinc to *N*-diphenylphosphinoyl arylimines with cyclic hydroxylamine ligands,[5e] namely, the hydroxy group of the chiral amino alcohol replaces one of the alkyl groups of dialkylzinc and the alcoholic oxygen atom coordinates with another equivalent of dialkylzinc to form the real reagent.[5e,17] Three chiral reagents (**10**–**12**) were modeled. All calculations were performed with the Gaussian 98 program.[18]

To search for all possible transition structures, a conformational search with the PM3[19] and HF/3-21G methods was first performed on four possible models (see the Supporting Information) with complex **10**. This resulted in 11 unique transition structures. All these transition structures are given in the Supporting Information. At the HF/3-21G level, the three most favorable transition structures are shown in Figure 1. Structure **13** is more stable than **14** and **15** by 2.9 and 4.1 kcal mol^{-1}, respectively. While **13** gives the *R* product, **14** and **15** lead to the formation of the *S* product.

Transition structures **13**–**15** were further calculated with the nonlocal density functional method of B3LYP/6-31G*,[20] which should give more reliable calculation results. Structure **13** is still the most stable. Structures **14** and **15** become less stable by 1.8 and 2.2 kcal mol^{-1}, respectively. Thus, the simple model calculations give results in qualitative agreement with the experimental observations, that is, the *R* product is formed preferentially.

All three transition structures have some similar features: the Me_2Zn attacks the C=N bond to form a four-membered-ring. The other zinc atom coordinates to the oxygen of the phosphinoyl group so that a six-membered-ring is fused with the four-membered-ring on one side and with a five-membered-ring on the other side. In **13**, the two methyl groups in the chiral ligand point upward and away from the $POMe_2$ group, and therefore there is little steric interaction. In **14**, the situation for the three fused rings is similar to that in **13**. Therefore, it does not have ring strain. However, the methyl group at the C1 position of the chiral amino alcohol points downward. It is close to one of the methyl groups of the $POMe_2$. The steric interaction between the two methyl groups, as shown by arrows in Figure 1, causes a significant destabilization. In **15**, the two methyl groups of the amino alcohol point away from the $POMe_2$, and therefore, do not

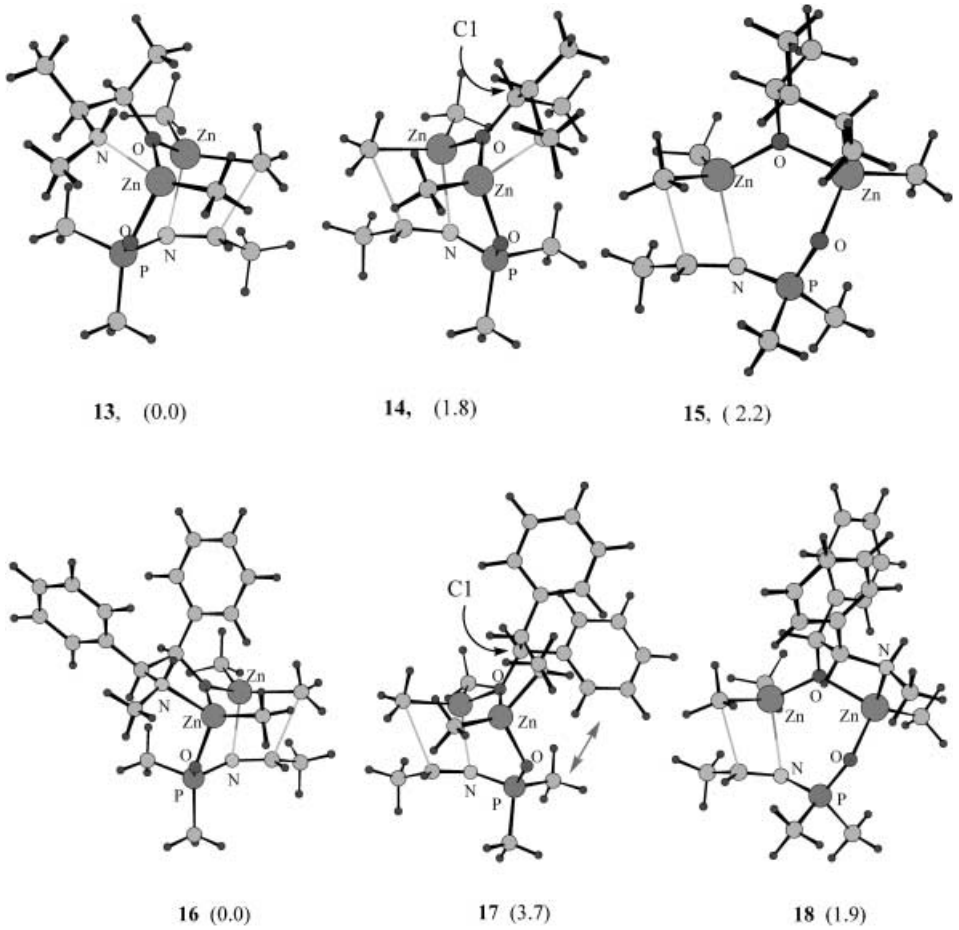


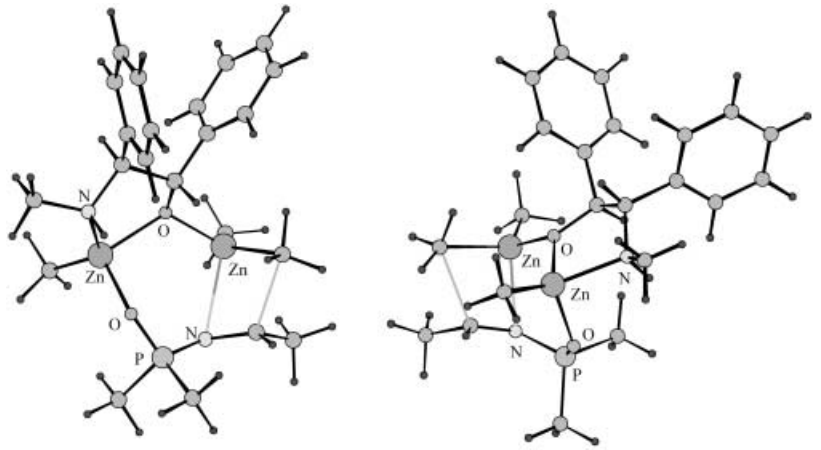
Figure 1. Calculated transition structures for the methylation of **9** by chiral complexes **10** and **11**. The calculated relative energies (B3LYP/6-31G*, kcal mol^{-1}) are given in parentheses.

participate in a steric interaction. However, the fusion of the three rings is not ideal. As can be seen, the N–P bond has rotated so that the P–O bond is nearly eclipsed with the Zn–N bond, which is being formed. In addition, the four-membered ring is not co-planar. The C-Zn-N-C dihedral angle is $\approx 30°$. Thus, this transition structure is destabilized by unfavorable ring strain.

Our next step was to change X from Me to Ph. The calculations only focused on the three favorable transition structures. As shown in Figure 1, the geometries of **16**, **17**, and **18** are quite similar to those of structures **13**, **14**, and **15**, respectively. The energy difference between **16** and **18** is about 1.9 kcal mol^{-1}, similar to that between **13** and **15**. However, structure **17** becomes destabilized, and is calculated to be about 3.7 kcal mol^{-1} less stable than **16**. This is apparently caused by the increased steric interaction between the downward phenyl group of the amino alcohol and the $POMe_2$ (as indicated by the arrow in **17** (Figure 1)). In the real substrate, the $POMe_2$ is replaced by $POPh_2$. This should not affect the relative stabilities between **16** and **18**. However, **17** is expected to be destabilized even further. Therefore, **17** can be ruled out. We can conclude that the formation of the *R* and *S* products is mainly determined by **16** and **18**, respectively. Since **18** is much less stable, it qualitatively rationalizes the generally high enantioselectivities observed experimentally for a variety of chiral amino alcohol ligands. It should be pointed out that, although we used $POMe_2$ instead of more sterically bulky $OPPh_2$, which is present in ligands **1**–**4**, the predicted stereoselectivity should not be affected because the two phenyl groups of the chiral amino alcohol ligand are far away from the group. Also because of this, the model of dimethylzinc for diethylzinc is reasonable.

We have also studied the transition structures with model ligand **12** to understand the reversed stereoselectivity with ligand **1f** observed experimentally. Again, many transition structures were explored. The most stable transition structures for the formation of the two enantiomeric products are given in Figure 2. The most stable transition structure for the formation of the *R* product is **19**. This structure is similar to structures **15** and **18**. Although the steric interactions involving the two phenyl groups of the chiral amino alcohol are avoided, the structure is destabilized by unfavorable ring fusion. The (H3)C-Zn-N-C dihedral angle is about 40° and the Zn-N-P-O dihedral angle is almost zero. The structure derived from **16** by changing the chirality of the C1 center is calculated to be less stable by about 3 kcal mol^{-1} as a result of severe steric interaction between the phenyl group attached to C1 and the spectator methyl group of the $ZnMe_2$. On the other hand, the most stable transition structure for the formation of the *S* product is **20**. This structure is very similar to structure **17**, except that the phenyl group attached to C1 has now swapped places with the hydrogen atom. Structure **17** is significantly destabilized by the steric interactions between the phenyl group and the $POMe_2$, but this steric interaction is absent in structure **20**. Thus, structure **20** is calculated to be more stable than structure **19** by about 0.6 kcal mol^{-1}. This result is in good agreement with the experimental observation with ligand **1f**. That is, ligand **1f** gives rise to an inversed configuration but low enantioselectivity compared to its chiral counterpart ligand **1b**.

A more detailed modeling of the substituent effect on the enantioselectivity using the real experimental chiral amino alcohol ligands would require much more elaborate calculations. Our calculations of simplified imine substrate, dialkylzinc, and chiral amino alcohol ligands do reveal the essential factors for the generally high enantioselectivity for the reactions studied experimentally. Our modeling of the chiral



19 (0.6 kcal mol^{-1}) *R* product

20 (0.0) *S* product

Figure 2. Calculated most stable transition structures for the formation of the *R* product **19** and the *S* product **20** of the addition of $ZnMe_2$ to imine **9** in the presence of a zinc complex of chiral amino alcohol model **12**. The calculated relative energies are given in parentheses.

amino alcohol ligands **4** also indicates high enantioselectivity (see the Supporting Information).

Conclusion

By screening *N*,*N*-disubstituted, *N*-monosubstituted amino alcohols and imino alcohols for the addition of diethylzinc to imines, we found that *N*-monosubstituted amino alcohols gave slightly higher enantioselectivities than their *N*,*N*-disubstituted counterparts. High enantioselectivities of up to 98% *ee* for addition of diethylzinc to imines were obtained with the very easily accessible ligand **3c**. So far, the highest enantioselectivities, ranging from 95% to 97% *ee* for the addition of dibutylzinc to imines, were observed with ligand **3c**. These results imply that the rigid and restricted structure of the amino alcohol was not the absolute requirement for the high enantioselective alkylation of diphenylphosphinoylimine with dialkylzinc. Studies on the transition states at the B3LYP/6-31G* level of theory revealed that the chiral amino alcohols promoted the reaction via the transition structure **16**. The accurate calculation to understand the reversed enantioselectivity with ligand **1f** resulted in a good agreement with the experimentally observed result. The calculation results indicated that higher enantioselectivity might also be achieved by the use of simpler chiral ligands and dimethylzinc.

Experimental Section

General: NMR spectra were recorded on a Brucker-200 or 300 MHz spectrometer. Elemental analyses were performed on a Carlo Erba-1106 Analyzer. EI mass spectra were recorded on a VG-7010E, and IR spectra on a NicroLab 200SXV. Optical rotation was measured with a PE polarmeter 341. HPLC analysis was performed on Beckman 110B chromatography with Beckman 168 variable wavelength detector. A Chiralpak AD column was purchased from Daicel Chemical Industries, Ltd. All reactions involving air- and moisture-sensitive compounds were carried out under a dry argon atmosphere with standard Schlenk line techniques. Toluene and THF were dried over sodium/benzophenone. CH_2Cl_2 was dried with CaH_2. Petroleum ether (PE) and ethyl acetate for column chromatography were distilled before use.

Materials: All starting materials were purchased from Acros and used directly.

General experimental for the preparation of (1*R*,2*S*)-*N*-aryl-1,2-diphenyl-2-aminoethanol (3a–m) and (1*R*,2*S*)-*N*-methyl-*N*-aryl-1,2-diphenyl-2-aminoethanol (2a–2g): A solution of (1*R*,2*S*)-1,2-diphenyl-2-aminoethanol (5 mmol) and the appropriate aryl aldehyde (5 mmol) in anhydrous ethanol was stirred for 2–12 h at room temperature, then sodium borohydride (8 mmol) was added. The reaction mixture was stirred for 2 h at room temperature, quenched with 2 M HCl, and the ethanol was removed by evaporation. The residue was neutralized with aqueous NaOH (0.5 M, 20 mL). The mixture was extracted with CH_2Cl_2 (3×20 mL), and the combined organic layers were washed with water (3×). The organic layer was dried over anhydrous sodium sulfate and evaporated to dryness under reduced pressure. Purification of the crude product by chromatography (silica) or by crystallization gave **3a–m**.

A mixture of **3** (3 mmol) and methanoic acid (5 mL) was stirred for 0.5 h at room temperature, and then aqueous formaldehyde (30%, 5 mL) was added. The mixture was refluxed for 10 h, and the remaining excess formaldehyde was removed with a rotary evaporator. The resulting residue was dissolved in NaOH (0.5 M, 10 mL), extracted with CH_2Cl_2(3× 15 mL), and the combined organic layers were washed with aqueous saturated NaCl. The organic layer was dried over anhydrous sodium sulfate, and evaporated to dryness under reduced pressure. Purification of the crude product by chromatography (silica) or by crystallization gave **2a–g**.

(1*R*,2*S*)-*N*-Methyl-*N*-4′-methoxylbenzyl-1,2-diphenyl-2-aminoethanol (2a): This compound was obtained as a white solid (0.991 g) in 95% yield; m.p. 83–84 °C; $[\alpha]_D^{25} = -68.5$ ($c = 1.01$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 2.28$ (s, 3H), 2.83–3.02 (brs, 1H), 3.29 (d, $J = 13.3$ Hz, 1H), 3.59–3.64 (m, 2H), 3.79 (s, 3H), 5.37 (d, $J = 5.6$ Hz, 1H), 6.77–7.24 ppm (m, 14H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 38.8$, 55.2, 58.8, 72.6, 74.4, 113.5, 126.6, 127.1, 127.4, 127.7, 127.8, 129.6, 129.9, 130.8, 135.9, 141.8, 158.6 ppm; IR (Nujol): $\tilde{\nu} = 3491$, 1611, 1514, 1459, 1251 (C-O-C), 700 (CH_2) cm^{-1}; MS (CI): *m*/*z* (%): 28, 77 $[C_6H_5]^+$, 91 $[PhCH_2]^+$, 121 $[C_8H_9O]^+$, 240 $[M+1-PhCH_2-OH]^+$; elemental analysis calcd (%) for $C_{23}H_{25}NO_2$: C 79.51, H 7.25, N 4.03; found: C 79.50, H 7.11, N 4.10.

(1*R*,2*S*)-*N*-Methyl-*N*-4′-benzoxylbenzyl-1,2-diphenyl-2-aminoethanol (2b): This compound was obtained as a white solid (1.143 g) in 90% yield; m.p. 93–94 °C; $[\alpha]_D^{25} = -58.0$ ($c = 1.00$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.30$ (s, 3H), 2.90 (brs, 1H), 3.27 (d, $J = 13.8$ Hz, 1H), 3.63 (m, 2H), 5.07 (s, 2H), 5.39 (d, $J = 5.7$ Hz, 1H), 6.88–7.46 ppm (m, 19H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 38.9$, 58.8, 70.0, 72.6, 74.5, 114.5, 126.5, 127.0, 127.4, 127.4, 127.7, 127.8, 127.9, 128.5, 129.5, 129.8, 131.2, 135.9, 137.1, 141.7, 157.8 ppm; IR (Nujol): $\tilde{\nu} = 3431$ (OH), 1511, 1459 (N-CH_3), 1237 (C-O-C), 1022 (C-O-C), 704 (CH_2) cm^{-1}; MS (EI): *m*/*z* (%): 91, (100) $[PhCH_2]^+$, 316 $[M+1-PhCH_2-OH]^+$, 197; elemental analysis calcd (%) for $C_{29}H_{29}NO_2$: C 82.24, H 6.90, N 3.31; found: C 82.23, H 7.00, N 3.45.

(1*R*,2*S*)-*N*-Methyl-*N*-2′,4′,6′-trimethylbenzyl-1,2-diphenyl-2-aminoethanol (2c): This compound was obtained as a white solid (1.002 g) in 93% yield; m.p. 95–96 °C; $[\alpha]_D^{25} = -66.7$ ($c = 1.01$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.17$ (s, 9H), 2.29 (s, 3H), 2.83–2.89 (brs, 1H), 3.46–3.57 (m, 2H), 3.71 (d, $J = 6.4$ Hz, 1H), 5.42 (d, $J = 6.4$ Hz, 1H),

6.8 (s, 2H), 7.19–7.36 ppm (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 19.9, 20.6, 36.4, 53. 6, 72.5, 76.9, 126.2, 126.8, 127.2, 127.5, 127.9, 128.0, 128.7, 129.4, 131.5, 135.7, 136.0, 137.8, 141.6 ppm; IR (Nujol): $\tilde{\nu}$ = 3532 (OH), 1611, 1455 (N-CH_3), 701 (CH_2) cm^{-1}; MS (EI): *m*/*z* (%): 77, 91, 133 (100), 252 (36); elemental analysis calcd (%) for $C_{25}H_{29}NO$: C 83.52, H 8.13, N 3.90; found: C 83.34, H 7.08, N 3.81.

(1*R*,2*S*)-*N*-Methyl-*N*-2′-bromobenzyl-1,2-diphenyl-2-aminoethanol (2d): This compound was obtained as a viscid liquid (1.069 g) in 90% yield; $[\alpha]_D^{25}$ = −33.7 (*c* = 0.986 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.31 (s, 3H), 2.90 (br s, 1H), 3.62–3.66 (m, 2H), 3.71 (d, *J* = 6.0 Hz, 1H), 5.42 (d, *J* = 6.0 Hz, 1H), 7.16–7.52 ppm (m, 14H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 39.1, 58.8, 69.9, 72.8, 75.2, 124.1, 126.6, 126.9, 127.2, 127.3, 127.5, 127.8, 127.9, 128.2, 129.0, 129.6, 130.5, 132.6, 135.9, 138.1, 141.7 ppm; IR (neat): $\tilde{\nu}$ = 3565, 3449 (OH), 1449 (N-CH_3), 703 (CH_2) cm^{-1}; MS (EI): *m*/*z* (%): 77, 91, 118, 169 (77) [$CH_2Ph^{79}Br$], 171 (77) [$CH_2Ph^{81}Br$], 288 (100) [*M*+1−$PhCH_2$−OH]$^+$, 290 (98); elemental analysis calcd (%) for $C_{22}H_{22}BrNO$: C 66.67, H 5.60, N, 3.53; found: C 66.56, H 5.66, N 3.64.

(1*R*,2*S*)-*N*-Methyl-*N*-3′-chlorobenzyl-1,2-diphenyl-2-aminoethanol (2e): This compound was obtained as a viscous liquid (0.895 g) in 85% yield; $[\alpha]_D^{25}$ = −135.9 (*c* = 0.504 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.06 (s, 3H), 2.68 (br s, 1H), 3.05 (d, *J* = 13.8 Hz, 1H), 3.37 (d, *J* = 13.8 Hz, 1H), 3.46 (d, *J* = 6.7 Hz, 1H), 5.06 (d, *J* = 6.7 Hz, 1H), 6.73–7.18 ppm (m, 14H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 34.8, 55.0, 68.8, 70.5, 122.6, 122.7, 123.1, 123.4, 123.6, 123.9, 124.0, 124.6, 125.4, 125.5, 130.1, 131.6, 137.3, 137.7 ppm; IR (neat): $\tilde{\nu}$ = 3563 (OH), 3446 (OH), 1596, 1450 (N-CH_3), 705 (CH_2) cm^{-1}; MS (EI): *m*/*z* (%): 42, 77, 91, 105, 118, 125 (100) [$CH_2Ph^{35}Cl$], 127 (33) [$CH_2Ph^{37}Cl$], 244 (80) [*M*+1−$PhCH_2$−OH]$^+$, 246 (26); elemental analysis calcd (%) for $C_{22}H_{22}ClNO$: C 75.09, H 6.30, N, 3.98; found: C 75.06, H 7.48, N 4.13.

(1*R*,2*S*)-*N*-Methyl-*N*-4′-chlorobenzyl-1,2-diphenyl-2-aminoethanol (2f): This compound was obtained as a white solid (0.896 g) in 85% yield; m.p. 102–103 °C; $[\alpha]_D^{25}$ = −65.0 (*c* = 1.01 in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.26 (s, 3H), 3.29 (d, *J* = 13.7 Hz, 1H), 3.58–3.66 (m, 2H), 5.35 (d, *J* = 6.30 Hz, 1H), 6.97–7.27 ppm (m, 14H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 38.7, 58.7, 72.6, 74.3, 126.6, 127.2, 127.6, 127.8, 127.9, 128.3, 129.5, 129.9, 132.5, 135.5, 137.4, 141.8 ppm; IR (Nujol): $\tilde{\nu}$ = 3488 (OH), 1401, 1455 (N-CH_3), 703 (CH_2) cm^{-1}; MS (EI): *m*/*z* (%): 77, 91, 118, 125 (100) [$CH_2Ph^{35}Cl$], 127(33) [$CH_2Ph^{37}Cl$], 244 (80) [*M*+1−$PhCH_2$−OH]$^+$, 246 (26); elemental analysis calcd (%) for $C_{22}H_{22}ClNO$: C 75.09, H 6.30, N, 3.98; found: C 75.08, H 6.29, N 4.04.

(1*R*,2*S*)-*N*-Methyl-*N*-piperonyl-1,2-diphenyl-2-aminoethanol (2g): This compound was obtained as a white solid (0.886 g) in 80% yield; m.p. 105–106 °C; $[\alpha]_D^{25}$ = −74.5 (*c* = 0.746 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.30 (s, 3H), 3.26 (d, *J* = 12.0 Hz, 1H), 3.57–3.67 (m, 2H), 5.40 (s, 1H), 5.95 (s, 2H), 6.70–6.73 (m, 3H) 7.14–7.28 ppm (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 38.7, 59.2, 72.7, 74.3, 100.8 (O-C-O),107.7, 109.0, 121.7, 126.5, 127.2, 127.4, 127.7, 127.8, 129.5, 129.8, 132.8, 135.8, 141.7, 146.4, 147.5 ppm (Ar); IR (Nujol): $\tilde{\nu}$ = 3484 (OH), 1489, 1448, 1450,1459, 1245, 1038, 705 cm^{-1}; MS (EI): *m*/*z* (%): 77, 91, 105, 135 (100) [$BnOCH_2O$]$^+$, 254 (39) [*M*+1−$PhCH_2$−OH]$^+$; elemental analysis calcd (%) for $C_{23}H_{23}NO_3$: C 76.43, H 6.41, N 3.88; found: C 76.18, H 6.37, N 4.00.

(1*R*,2*S*)-*N*-4′-Methoxylbenzyl-1,2-diphenyl-2-aminoethanol (3a): This compound was obtained as a white solid (1.249 g) in 75% yield; m.p. 156–158 °C; $[\alpha]_D^{25}$ = +18.9 (*c* = 1.02 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.26 (d, *J* = 13.1 Hz, 1H), 3.68 (d, *J* = 13.1 Hz, 1H), 3.81 (s, 3H), 3.94 (d, *J* = 5.7 Hz, 1H), 4.87 (d, *J* = 5.7 Hz, 1H), 6.84 (d, *J* = 8.7 Hz, 2H), 7.09–7.31 ppm (m, 12H); ^{13}C NMR (75 MHz, DMSO): δ = 50.0, 55.3, 67.5, 76.6, 113.8, 126.9, 127.2, 127.3, 127.8, 128.9, 129.2, 132.8, 141.3, 143.6, 158.3 ppm (Ar); IR (Nujol): $\tilde{\nu}$ = 3085, 3028, 1611, 1513, 1452 (O-CH_3), 1247 (C-O-C), 699 (CH_2) cm^{-1}; MS (EI): *m*/*z* (%): 121 [C_8H_9O]$^+$, 226 [*M*+1−$PhCH_2$−OH]$^+$, 334 [*M*+1]; elemental analysis calcd (%) for $C_{22}H_{23}NO_2$: C 79.25, H 6.95, N 4.20; found: C 78.95, H 6.88, N 4.46.

(1*R*,2*S*)-*N*-4′-Benzoxylbenzyl-1,2-diphenyl-2-aminoethanol (3b): This compound was obtained as a white solid (1.452 g) in 71% yield; m.p. 182–183 °C; $[\alpha]_D^{25}$ = +18.3 (*c* = 0.378 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.53 (d, *J* = 13.1 Hz, 1H), 3.73 (d, *J* = 13.1 Hz, 1H), 3.96 (d, *J* = 5.4 Hz, 1H), 4.97 (s, 1H), 5.03 (s, 2H), 6.91(d, *J* = 8.7 Hz, 2H), 7.11–7.43 ppm (m, 19H); ^{13}C NMR (75 MHz, DMSO): δ = 50.2, 67.8, 70.0, 78.4, 114.6, 115.3, 126.9, 127.2, 127.4, 127.6, 127.7, 127.8, 127.9, 128.2, 128.4, 128.6, 128.7, 128.8, 129.2, 137.3, 140.7, 142.9, 157.5 ppm; IR (Nujol): $\tilde{\nu}$ = 3082, 3028, 1513, 1611, 1451, 1248 (C-O-C), 1010 (C-O-C), 699 (CH_2) cm^{-1}; MS (CI) *m*/*z* (%): 91 [$PhCH_2$]$^+$, 197 [CH_2PhOBn]$^+$, 302 [*M*+1−$PhCH_2$−OH]$^+$; elemental analysis calcd (%) for $C_{28}H_{27}NO_2$: C 82.12, H 6.65, N 3.42; found: C 82.39, H 6.75, N 3.61.

(1*R*,2*S*)-*N*-2′,4′,6′-Trimethylbenzyl-1,2-diphenyl-2-aminoethanol (3c): This compound was obtained as a white solid (1.259 g) in 73% yield; m.p. 124–125 °C; $[\alpha]_D^{25}$ = +9.6 (*c* = 1.00 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.16 (s, 6H), 2.26 (s, 3H), 3.54 (d, *J* = 11.6 Hz, 1H), 3.62 (d, *J* = 11.6 Hz, 1H), 3.98 (d, *J* = 6.4 Hz, 1H), 4.79 (d, *J* = 6.4 Hz, 1H), 6.83 (s, 2H), 7.19–7.37 ppm (m, 10H); ^{13}C NMR (75 MHz, DMSO): δ = 19.0, 20.8, 45.1, 70.0, 77.1, 127.1, 127.4, 127.9, 128.1, 128.7, 128.8, 133.9, 135.7, 136.7, 142.2, 143.8 ppm; IR (Nujol): $\tilde{\nu}$ = 3395 (OH), 3341, 3061, 3032, 1454, 702 (CH_2) cm^{-1}; MS (EI): *m*/*z* (%): 106 [PHCHO]$^+$, 133 [CH_2 (2,4,6-trimethyl benzene)], 238 [*M*+1−$PhCH_2$−OH]$^+$, 346 [*M*+1]; elemental analysis calcd (%) for $C_{24}H_{27}NO$: C 83.44, H 7.88, N 4.05; found: C 83.30, H 7.93, N 4.28.

(1*R*,2*S*)-*N*-2′-Bromobenzyl-1,2-diphenyl-2-aminoethanol (3d): This compound was obtained as a white solid (1.489 g) in 78% yield; m.p. 147–148 °C; $[\alpha]_d^{25}$ = +27.9 (*c* = 0.82 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.64 (d, *J* = 13.6 Hz, 1H), 3.79 (d, *J* = 13.6 Hz, 1H), 3.89 (d, *J* = 6.0 Hz, 1H), 4.86 (d, *J* = 6.0 Hz, 1H), 7.11–7.50 ppm (m, 14H); ^{13}C NMR (75 MHz, DMSO and $CDCl_3$): δ = 50.8, 67.9, 76.9, 123.5, 127.0, 127.2, 127.3, 127.6, 127.8, 127.8, 128.8, 128.9, 130.3, 132.5, 139.3, 140.8, 143.0 ppm; IR (Nujol): $\tilde{\nu}$ = 3301, 3189, 3086, 3064, 3030, 1452, 702 (CH_2) cm^{-1}; MS (EI): *m*/*z* (%): 77, 91, 118, 169 [$CH_2Ph^{79}Br$−1], 171 [$CH_2Ph^{81}Br$−1], 274 [*M*+1−$PhCH_2$−OH]$^+$, 276; elemental analysis calcd (%) for $C_{21}H_{20}BrNO$: C 65.98, H 5.27, N 3.66; found: C 66.08, H 5.27, N 4.01.

(1*R*,2*S*)-*N*-4′-Bromobenzyl-1,2-diphenyl-2-aminoethanol (3e): This compound was obtained as a white solid (1.165 g) in 61% yield; m.p. 179–180 °C; $[\alpha]_D^{29}$ = +23.5 (*c* = 0.51 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.06–2.75 (br s, 2H), 3.50 (d, *J* = 13.2 Hz, 1H), 3.70 (d, *J* = 13.2 Hz, 1H), 3.90 (d, *J* = 5.7 Hz, 1H), 4.86 (d, *J* = 5.4 Hz, 1H), 7.03–7.42 ppm (m, 14H); ^{13}C NMR (75 MHz, DMSO): δ = 54.5, 66.4, 75.0, 117.2, 131.5, 131.9, 132.4, 132.6, 133.0, 133.5, 133.6, 147.5, 154.3 ppm; IR (Nujol): $\tilde{\nu}$ = 3314, 3029 cm^{-1}; MS (EI) *m*/*z* (%): 169 [$CH_2Ph^{79}Br$−1], 171 [$CH_2Ph^{81}Br$−1], 274 [*M*+1−$PhCH_2$−OH]$^+$, 276, 277; 362 [*M*−H_2O]; elemental analysis calcd (%) for $C_{21}H_{20}BrNO$: C 65.98, H 5.27, N 3.66; found: C 65.83, H 5.24, N 3.66.

(1*R*,2*S*)-*N*-2′-Chlorobenzyl-1,2-diphenyl-2-aminoethanol (3f): This compound was obtained as a white solid (1.249 g) in 75% yield; m.p. 142–143 °C; $[\alpha]_D^{25}$ = +21.0 (*c* = 1.01 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.70 (d, *J* = 13.7 Hz, 1H), 3.79 (d, *J* = 13.7 Hz, 1H), 3.90–3.95 (m, 1H), 4.95–5.0 (m, 1H), 7.11–7.32 ppm (m, 14H); ^{13}C NMR (75 MHz, DMSO and $CDCl_3$): δ = 48.1, 67.9, 76.3, 110.3, 113.5, 117.3, 117.6, 118.1, 126.2, 126.8, 127.2, 127.7, 127.9, 128.5, 128.9, 129.1, 129.4, 130.4, 133.0, 143.2 ppm; IR (Nujol): $\tilde{\nu}$ = 3306, 3250, 3182 cm$^{-1;}$ MS (EI): *m*/*z* (%): 125 [$CH_2Ph^{35}Cl$], 127 [$CH_2Ph^{37}Cl$], 230 [*M*+1−$PhCH_2$−OH]$^+$, 232, 233, 319 [*M*−H_2O], 321; elemental analysis calcd (%) for $C_{21}H_{20}ClNO$: C 74.66, H 5.97, N 4.15; found: C 74.47, H 6.08, N 4.53.

(1*R*,2*S*)-*N*-3′-Chlorobenzyl-1,2-diphenyl-2-aminoethanol (3g): This compound was obtained as a white solid (1.146 g) in 68% yield; m.p. 152–153 °C; $[\alpha]_D^{25}$ = +24.4 (*c* = 0.814 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.51 (d, *J* = 13.7 Hz, 1H,), 3.71(d, *J* = 13.7 Hz, 1H), 3.90 (d, *J* = 6.0 Hz, 1H), 4.87 (d, *J* = 6.0 Hz, 1H), 7.04–7.34 ppm (m, 14H); ^{13}C NMR (75 MHz, DMSO and $CDCl_3$): δ = 54.9, 72.6, 81.5, 131.1, 131.4, 131.7, 131.9, 132.2, 132.6, 133.5, 134.5, 138.3, 145.3, 147.6, 147.9 ppm; IR (Nujol): $\tilde{\nu}$ = 3317 (OH), 3085, 3030, 1401, 1451, 1426, 703 (CH_2) cm^{-1}; MS (EI): *m*/*z* (%): 91, 125 [$CH_2Ph^{35}Cl$], 127 [$CH_2Ph^{37}Cl$], 230 [M^{35}+1−$PhCH_2$−OH]$^+$, 232 [M^{37}+1−$PhCH_2$−OH]$^+$, 338 [*M*+1]; elemental analysis calcd (%) for $C_{21}H_{20}ClNO$: C 74.66, H 5.97, N 4.15; found: C 74.54, H 6.02, N 4.43.

(1*R*,2*S*)-*N*-4′-Chlorobenzyl-1,2-diphenyl-2-aminoethanol (3h): This compound was obtained as a white solid (1.095 g) in 65% yield; m.p. 174–175 °C; $[\alpha]_D^{25}$ = +25.0 (*c* = 0.79 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.53 (d, *J* = 13.5 Hz, 1H), 3.76 (d, *J* = 13.5 Hz, 1H), 3.91 (d, *J* = 5.7 Hz, 1H), 4.96 (d, *J* = 3.6 Hz, 1H), 7.10–7.32 ppm (m, 14H);

^{13}C NMR (75 MHz, DMSO and $CDCl_3$): δ = 54.6, 72.5, 81.3, 131.7, 131.9, 131.9, 132.4, 132.5, 132.9, 133.6, 134.4, 136.3, 144.4, 145.5, 147.9 ppm; IR (Nujol): $\tilde{\nu}$ = 3310 (OH), 3085, 3028, 1400, 701 (CH_2) cm^{-1}; MS (EI): *m*/*z* (%): 125 [$CH_2Ph^{35}Cl$], 127 [$CH_2Ph^{37}Cl$], 230 [M^{35}+1−PhCH$_2$−OH]$^+$, 232 [M^{37}+1−PhCH$_2$−OH]$^+$, 338 [*M*+1]; elemental analysis calcd (%) for $C_{21}H_{20}ClNO$: C 74.66, H 5.97, N 4.15; found: C 74.44, H 6.04, N 4.36.

(1*R*,2*S*)-*N*-2′,6′-Dichlorobenzyl-1,2-diphenyl-2-aminoethanol (3i): This compound was obtained as white crystals in 39% yield; m.p. 113–114 °C; $[\alpha]_d^{25}$ = +13.0 (*c* = 1.00 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.15 (brs, 1H,), 3.13 (brs, 1H), 3.88–4.03 (m, 3H) 4.83 (d, *J* = 6.0 Hz, 1H), 7.08–7.29 ppm (m, 13H); ^{13}C NMR (75 MHz, DMSO): δ = 46.6, 68.3, 126.8, 127.6, 128.0, 128.2, 128.3, 128.9, 135.3, 135.9, 139.1, 140.2 ppm; IR (Nujol): $\tilde{\nu}$ = 3332, 3304 cm^{-1}; MS (CI): *m*/*z* (%): 159 [$CH_2Ph^{35}Cl^{35}Cl$], 161 [$CH_2Ph^{37}Cl^{37}Cl$], 264 [M^{35}+1−PhCH$_2$−OH]$^+$, 266 [M^{37}+1−PhCH$_2$−OH]$^+$, 355, 371 [M^{35}+1]; elemental analysis calcd (%) for $C_{21}H_{19}Cl_2NO$: C 67.75, H 5.14, N 3.76; found: C 67.75, H 5.31, N 4.05.

(1*R*,2*S*)-*N*-Piperonyl-1,2-diphenyl-2-aminoethanol (3j): This compound was obtained as a white solid; m.p. 134–135 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.47 (d, *J* = 13.2 Hz, 1H), 3.65 (d, *J* = 13.2 Hz, 1H), 3.94 (d, *J* = 5.4 Hz, 1H), 4.89 (d, *J* = 5.7 Hz, 1H), 5.94 (s, 2H), 6.60–7.31 ppm (m, 13H); ^{13}C NMR (75 MHz, DMSO): δ = 50.7, 67.6, 100.8, 107.9,108.6, 121.2, 126.0, 126.7, 126.8, 126.6, 127.8, 127.9, 128.0, 128.2, 128.3, 133.4, 138.7, 140.3, 146.5, 146.5, 147.6 ppm; IR (Nujol): $\tilde{\nu}$ = 3313, 3088, 3027, 1254 (C-O-C), 1042 (C-O-C) cm^{-1}; MS (EI): *m*/*z* (%): 135 (100) [BnOCH$_2$O]$^+$, 240 (100) [*M*+1−PhCH$_2$−OH]$^+$, 241, 348 [*M*+1]; elemental analysis calcd (%) for $C_{22}H_{21}NO_3$: C 76.06, H 6.09, N 4.03; found: C 76.06, H 6.39, N 3.90.

(1*R*,2*S*)-*N*-4′-Methylbenzyl-1,2-diphenyl-2-aminoethanol (3k): This compound was obtained as white crystals in 64% yield; m.p.167–168 °C; $[\alpha]_D^{25}$ = +14.7 (*c* = 1.03 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.33 (s, 3H), 3.54 (d, *J* = 13.5 Hz, 1H), 3.71 (d, *J* = 13.5, 1H), 3.96(d, *J* = 5.4 Hz, 1H) 4.83 (d, *J* = 5.4 Hz, 1H), 7.07–7.29 ppm (m, 14H); ^{13}C NMR (75 MHz, DMSO and $CDCl_3$): δ = 21.0, 50.5, 67.8, 76.6, 111.2, 115.9, 119.2, 120.2, 120.5, 125.8, 126.9, 127.2, 127.8, 128.0, 128.9, 135.8, 137.7, 141.2, 143.4, 155.5 ppm; IR (Nujol): $\tilde{\nu}$ = 3315, 3059, 3024 cm^{-1}; MS (EI): *m*/*z* (%): 105, 210 [*M*+1−PhCH$_2$−OH]$^+$, 211 [*M*+1−PhCH$_2$−OH]$^+$, 318 [*M*+1]; elemental analysis calcd (%) for $C_{22}H_{23}NO$: C 82.24, H 7.30, N 4.41; found: C 83.21, H 7.52, N 4.59.

(1*R*,2*S*)-*N*-Furyl-1,2-diphenyl-2-aminoethanol (3l): This compound was obtained as white crystals in 73.2% yield; m.p. 133–134 °C; $[\alpha]_D^{25}$ = +32.1 (*c* = 1.00 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.56 (d, *J* = 14.6 Hz, 1H), 3.75 (d, *J* = 14.6 Hz, 1H), 3.92 (d, *J* = 6.0 Hz, 1H), 4.90 (d, *J* = 6.0 Hz, 1H), 6.08 (d, *J* = 3.0 Hz, 1H), 6.29 (dd, *J* = 2.9, 1.9 Hz, 1H), 7.12–7.34 ppm (m, 11H); ^{13}C NMR (75 MHz, DMSO): δ = 43.4, 67.5, 76.5, 106.9, 110.4, 127.1, 127.2, 127.8, 128.9, 140.4, 141.9, 14.9, 154.0 ppm; IR (Nujol): $\tilde{\nu}$ = 3324, 3060, 3030 cm^{-1}; elemental analysis calcd (%) for $C_{19}H_{19}NO_2$: C 77.79, H 6.53, N 4.77; found: C 77.61, H 6.54, N 4.67.

(1*R*,2*S*)-*N*-α-Naphthyl-1,2-diphenyl-2-aminoethanol (3m): This compound was obtained as a white solid; m.p. 141–142 °C; $[\alpha]_D^{25}$ = +14.3 (*c* = 1.00 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.99 (d, *J* = 12.8 Hz, 1H), 4.05 (d, *J* = 5.9 Hz, 1H), 4.16(d, *J* = 13.0 Hz, 1H), 4.86 (d, *J* = 6.0 Hz, 1H), 7.10–7.88 ppm (m, 17H); ^{13}C NMR (75 MHz, DMSO and $CDCl_3$): δ = 49.0, 68.8, 76.6, 124.0, 125.7, 125.9, 126.1, 126.2, 127.1, 127.2, 127.3, 127.6, 127.8, 127.9, 128.7, 129.0, 131.7, 133.6, 136.4 ppm; IR (Nujol): $\tilde{\nu}$ = 3316 (OH), 3170, 3045, 1452, 1416, 710 (CH_2) cm^{-1}; MS (EI): *m*/*z* (%): 106, 141, 194, 246 [*M*+1−PhCH$_2$−OH]$^+$, 354 [*M*+1]; elemental analysis calcd (%) for $C_{21}H_{20}ClNO$: C 84.95, H 6.56, N 3.96; found: C 85.05, H 6.50, N 3.87.

General procedure for the preparation of (1*R*,2*S*)-*N*-aryl-1,2-diphenylidene-2-aminoethanol (4a–m): A solution of (1*R*,2*S*)-1,2-diphenyl-2-aminoethanol (2.35 mmol) and aryl aldehyde (2.50 mmol) in anhydrous ethanol (20 mL) was stirred for 2–12 h at room temperature. The solvent was removed to give the crude product as a white solid that was purified by crystallization in *n*-hexane to give **4a–m**.

(1*R*,2*S*)-*N*-4′-Methoxylbenzylidene-1,2-diphenyl-2-aminoethanol (4b): This compound was obtained as white crystals (550 mg) in 68.5% yield; m.p. 130–131 °C; $[\alpha]_D^{25}$ = −27.4 (*c* = 1.01, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.80 (brs, 1H), 3.85 (s, 3H), 4.50 (d, *J* = 6.0 Hz, 1H), 5.09 (d, *J* = 6.0 Hz, 1H), 6.92 (d, *J* = 8.64 Hz, 2H), 7.23–7.40 (m, 10H), 7.68 (d, *J* = 8.7 Hz, 2H), 8.07 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.3, 78.2, 80.8, 113.8, 114.3, 127.1, 127.4, 127.5, 127.56, 127.7, 128.0, 128.1, 128.2, 128.4, 129.1, 129.8, 140.3, 140.7, 161.7 ppm; IR (Nujol): $\tilde{\nu}$ = 3389 (OH), 3032 (Ar-C-H), 1644 (Ar-C=N), 1606, 1513, 1455, 1257, 699 cm^{-1}; HRMS calcd for $C_{22}H_{22}NO_2$: 332.1645, found 332.1650.

(1*R*,2*S*)-*N*-2′,4′,6′-Trimethylbenzylidene-1,2-diphenyl-2-aminoethanol (4c): This compound was obtained as white crystals (682 mg) in 84.6% yield; m.p. 115 °C; $[\alpha]_D^{25}$ = −40.5 (*c* = 0.50 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.18 (s, 6H), 2.26 (s, 3H), 2.42 (brs, 1H), 4.48 (d, *J* = 6.9 Hz, 1H), 5.05 (d, *J* = 6.9 Hz, 1H), 6.82 (s, 2H), 7.27–7.48 (m, 10H), 8.40 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.5, 21.0, 78.3, 83.2, 127.3, 127.5, 127.6, 128.0, 128.3, 128.3, 129.3, 130.4, 137.7, 138.9, 140.6, 140.8, 162.1 ppm; IR (Nujol): $\tilde{\nu}$ = 3368 (OH), 3306, 3031 (Ar-C-H), 1646 (Ar-C=N) cm^{-1}; MS (EI): *m*/*z* (%): 236 (100) [*M*−PhCH$_2^+$−H$_2$O], 237 [*M*+1−PhCH$_2$−H$_2$O]$^+$, 343 [*M*]$^+$; elemental analysis calcd (%) for $C_{24}H_{25}NO$: C 83.93, H 7.34, N 4.08; found: C 83.92, H 7.26, N 4.10.

(1*R*,2*S*)-*N*-3′-Methylbenzylidene-1,2-diphenyl-2-aminoethanol (4d): This compound was obtained as white crystals in 78.5% yield; m.p. 74 °C; $[\alpha]_D^{25}$ = −22.4 (*c* = 0.49 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.39 (s, 3H), 2.60 (brs, 1H), 4.50 (d, *J* = 6.0 Hz, 1H), 5.09 (d, *J* = 6.0 Hz, 1H), 7.26–7.39 (m, 12H), 7.48 (d, 1H), 7.56 (s, 1H), 8.08 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.2, 78.1, 81.0,125.6, 127.1, 127.4, 127.7, 128.1, 128.3, 128.3, 128.6, 131.6, 136.0, 138.1, 140.1, 140.6, 162.0 ppm; IR (Nujol): $\tilde{\nu}$ = 3392 (OH), 3347, 3029 (Ar-C-H), 1647 (Ar-C=N) cm^{-1}; HRMS calcd for $C_{22}H_{22}NO$: 316.1696, found 316.1693.

(1*R*,2*S*)-*N*-3′-Chlorobenzylidene-1,2-diphenyl-2-aminoethanol (4e): This compound was obtained as a white solid (684 mg) in 87.3% yield; m.p. 83–84 °C; $[\alpha]_D^{25}$ = +3.4 (*c* = 1.00 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.18 (brs, 1H), 4.18 (d, *J* = 6.4 Hz, 1H), 4.76 (d, *J* = 6.4 Hz, 1H), 6.92–7.12 (m, 11H), 7.22–7.25 (m, 2H), 7.59 (s, 1H), 7.68 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 78.1, 81.1, 126.5, 126.6, 127.1, 127.2, 127.4, 127.6, 127.6, 127.7, 127.8, 127.9, 128.3, 128.3, 129.7, 130.6, 134.6, 137.7, 140.4, 140.5, 160.2 ppm; IR (Nujol): $\tilde{\nu}$ = 3440 (OH), 3032 (Ar-C-H),1633 (Ar-C=N) cm^{-1}; HRMS calcd for $C_{21}H_{19}NO^{35}Cl$: 336.1150, found 336.1149.

(1*R*,2*S*)-*N*-4′-Chlorobenzylidene-1,2-diphenyl-2-aminoethanol (4f): This compound was obtained as a white solid (672 mg) in 81.0% yield; m.p. 91–92 °C; $[\alpha]_D^{25}$ = +8.7 (*c* = 1.03 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.49 (brs, 1H), 4.49 (d, *J* = 6.4 Hz, 1H), 5.07 (d, *J* = 6.4 Hz, 1H), 7.26–7.42 (m, 12H), 7.63 (d, *J* = 8.3 Hz, 2H), 8.02 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 78.1, 81.1, 126.5, 127.2, 127.4, 127.5, 127.6, 127.7, 127.8, 127.9, 128.3, 128.3, 128.5, 128.7, 129.4, 1340.5, 136.7, 140.1, 140.6, 160.4 ppm; IR (Nujol): $\tilde{\nu}$ = 3382 (OH), 3029 (Ar-C-H), 1646 (Ar-C=N) cm^{-1}; HRMS calcd for $C_{21}H_{19}NO^{35}Cl$: 336.1150, found 336.1154.

(1*R*,2*S*)-*N*-2′-Bromobenzylidene-1,2-diphenyl-2-aminoethanol (4g): This compound was obtained as white crystals (589 mg) in 63.0% yield; m.p. 133–134 °C; **4g** $[\alpha]_D^{20}$ = + 9.4 (c = 1.00 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.52 (brs, 1H), 4.59 (d, *J* = 6.3 Hz, 1H), 5.08 (d, *J* = 6.3 Hz, 1H), 7.24–7.53 (m, 13H), 8.05–8.08 (m, 1H), 8.44 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 78.2, 81.2, 125.1, 127.1, 127.4, 127.4, 127.5, 127.6, 127.6, 127.7, 127.7, 127.9, 128.3, 128.3, 128.9, 131.8, 132.9, 134.4, 140.4, 140.5, 160.8 ppm (C=N); IR (Nujol): $\tilde{\nu}$ = 3386 (OH), 3330, 3031 (Ar-C-H), 1638 (Ar-C=N) cm^{-1}; MS (EI): *m*/*z* (%): 77, 89, 91, 165 (79), 169 [$CH_2Ph^{79}Br$], 171 [$CH_2Ph^{81}Br$], 193 273 (100) [*M*−PhCH$_2$−H$_2$O]$^+$, 274 (55) [*M*+1−PhCH$_2$−H$_2$O]$^+$ 380 [*M*]$^+$; elemental analysis calcd (%) for $C_{21}H_{18}BrNO$: C 66.33, H 4.77, N 3.68; found: C 66.38, H 4.83, N 3.68.

(1*R*,2*S*)-*N*-3′-Bromobenzylidene-1,2-diphenyl-2-aminoethanol (4h): This compound was obtained as white crystals (475 mg) in 53.2% yield; m.p. 88 °C; $[\alpha]_D^{25}$ = −2.1 (*c* = 0.99 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.18 (brs, 1H), 4.18 (d, *J* = 6.4 Hz, 1H), 4.76 (d, *J* = 6.4 Hz, 1H), 6.92–7.11 (m, 11H), 7.22–7.25 (m, 2H). 7.59 (s, 1H), 7.68 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 78.1, 81.2, 122.7, 127.1, 127.1, 127.6, 127.7, 127.8, 128.3, 130.0, 130.7, 133.6, 138.0, 140.0, 140.5, 160.1 ppm (C=N); IR (Nujol): $\tilde{\nu}$ = 3468 (OH), 3032 (Ar-C-H), 1631 (Ar-C=N); HRMS calcd for $C_{21}H_{19}NO^{79}Br$: 380.0644, found 380.0651.

(1*R*,2*S*)-*N*-4′-Bromobenzylidene-1,2-diphenyl-2-aminoethanol (4i): This compound was obtained as white crystals (641 mg) in 68.5% yield; m.p. 104–105 °C; $[\alpha]_D^{25} = +8.2$ ($c = 1.06$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.49$ (brs, 1H), 4.48 (d, $J = 6.3$ Hz, 1H), 5.06 (d, $J = 6.3$ Hz, 1H), 7.25–7.58 (m, 14H), 8.00 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 78.1, 81.1, 125.1, 127.1, 127.5, 127.6, 127.8, 128.3, 129.6, 131.7, 134.9, 140.0, 140.5, 160.5$ ppm; IR (Nujol): $\tilde{\nu} = 3389$ (OH), 3031(Ar-C-H), 1647 (Ar-C=N) cm^{-1}; HRMS calcd for $C_{21}H_{19}NO^{79}Br$: 380.0644, found 380.0653.

(1*R*,2*S*)-*N*-4′-Benzoxylbenzylidene-1,2-diphenyl-2-aminoethanol (4j): This compound was obtained as white crystals (700 mg) in 74.8% yield; m.p. 109.9 °C; $[\alpha]_D^{25} = -19.6$ ($c = 0.50$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.48$ (brs, 1H), 4.48 (d, $J = 6.0$ Hz, 1H), 5.07 (d, $J = 6.0$ Hz, 1H), 5.11(s, 2H), 7.00 (d, $J = 8.7$ Hz, 2H), 7.25–7.44 (m, 10H), 7.68 (d, $J = 8.4$ Hz, 2H), 8.06 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 69.9, 78.2, 80.8, 114.7, 126.9, 127.1, 127.4, 127.4, 127.5, 127.7, 128.1, 128.2, 128.4, 128.6, 129.3, 129.8, 136.5, 140.3, 140.7, 161.0$ ppm; IR (Nujol): $\tilde{\nu} = 3378$ (OH), 3031(Ar-C-H), 1640 (Ar-C=N) cm^{-1}; HRMS calcd for $C_{28}H_{26}NO_2$: 408.1958, found 408.1965.

(1*R*,2*S*)-*N*-(4′-*N*,*N*-Dimethylbenzylidene)-1,2-diphenyl-2-aminoethanol (4k): This compound was obtained as pale yellow crystals (670 mg) in 83.0% yield; m.p. 119–120 °C; $[\alpha]_D^{25} = -79.2$ ($c = 0.94$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 3.03$ (s, 6H), 4.47 (d, $J = 5.7$ Hz, 1H), 5.07 (d, $J = 5.7$ Hz, 1H), 6.69 (d, $J = 8.7$ Hz, 2H), 7.19–7.29 (m, 10H), 7.62 (d, $J = 8.7$ Hz, 2H), 8.04 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 40.1, 78.2, 80.5, 111.4, 124.3, 126.9, 127.1, 127.5, 127.6, 127.7, 127.9, 128.0, 128.2, 128.4, 129.7, 140.4, 140.8, 152.1, 161.5$ ppm; IR (Nujol): $\tilde{\nu} = 3438$ (OH), 3029(Ar-C-H), 1646 (Ar-C=N), 1606 cm^{-1}; HRMS calcd for $C_{23}H_{25}N_2O$: 345.1961, found 345.1950.

(1*R*,2*S*)-*N*-Piperonylidene-1,2-diphenyl-2-aminoethanol (4l): This compound was obtained as white crystals (520 mg) in 65.5% yield; m.p. 105–106 °C; $[\alpha]_D^{25} = -31.4$ ($c = 1.00$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.26$ (brs, 1H), 4.46 (d, $J = 6.3$ Hz, 1H), 5.05 (d, $J = 6.3$ Hz, 1H), 6.00 (s, 2H), 6.79 (d, $J = 7.8$ Hz, 1H), 7.01(d, $J = 7.8$ Hz, 1H) 7.25–7.41 (m, 11H), 7.97 (s, 1H), 8.03 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 78.2, 80.7, 101.3, 106.5, 107.9, 124.6, 126.9, 127.1, 127.5, 128.1, 128.3, 130.9, 140.3, 140.7, 148.1, 149.9, 160.8$ ppm (C=N); IR (Nujol): $\tilde{\nu} = 3410$ (OH), 3333, 3030(Ar-C-H), 1638 (Ar-C=N) cm^{-1}; HRMS calcd for $C_{22}H_{20}NO_3$: 346.1438, found 346.1427.

(1*R*,2*S*)-*N*-(α-Naphthylidene)-1,2-diphenyl-2-aminoethanol (4m): This compound was obtained as a white solid (350 mg) in 42.1% yield; m.p. 108 °C; $[\alpha]_D^{25} = -9.7$ ($c = 0.50$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.56$ (brs, 1H), 4.62 (d, $J = 6.6$ Hz, 1H), 5.17 (d, $J = 6.6$ Hz, 1H), 7.27–7.90 (m, 16H), 8.69 (s, 1H), 8.71 ppm (d, $J = 7.3$ Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 78.4, 82.6, 124.6, 125.2, 126.0, 127.1, 127.4, 127.5, 127.6, 127.9, 128.4, 128.5, 128.5, 129.4, 131.2, 131.2, 131.5, 133.7, 140.6, 140.9, 162.0$ ppm; IR (Nujol): $\tilde{\nu} = 3528$ (OH), 3458, 3030 (Ar-C-H), 1638 (Ar-C=N) cm^{-1}; HRMS calcd for $C_{25}H_{22}NO$: 352.1696, found 352.1691.

Enantioselective addition of diethylzinc to *N*-diphenylphosphinoyl benzalimine: Typical experimental procedure for the enantioselective addition of diethylzinc to *N*-diphenylphosphinoyl benzalimine (**5a**, 0.1 mmol) in the presence of **3c** (0.1 mmol): Imine **5a** (30.5 mg, 0.1 mmol) and amino alcohol **3c** (34.5 mg, 0.1 mmol) were dissolved in toluene (2 mL) under argon. To the mixture was added Et_2Zn in hexane (1 M, 0.5 mL, 0.5 mmol) at room temperature. After the reaction mixture had been stirred for 48 h, the reaction was quenched with saturated aqueous ammonium chloride, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was purified by column chromatography (silica gel) to give **6a** as a white solid (30.8 mg). Yield: 92%; $[\alpha]_D^{15} = +34.55$ ($c = 1.01$ in acetone); the enantiomeric excess of 97% with the *R* isomer as the major product was determined by HPLC (Chiracel AD column, hexane/propan-2-ol 80:20 ; flow rate 1 mL min^{-1}; *R* isomer, t_R 8.66 min and *S* isomer, t_R 11.60 min*)*.

Enantioselective addition of diethylzinc to *N*-diphenylphosphinoyl benzalimine (4a, 1 mmol) in the presence of 3c (1 mmol): Imine **5a** (305.0 mg, 1 mmol) and amino alcohol **3c** (345.1 mg, 1 mmol) were dissolved in toluene (20 mL) under argon. Et_2Zn in hexane (1 M, 5 mL, 5 mmol) was added dropwise to the mixture at 0–5 °C. After the reaction mixture had been stirred for 48 h at room temperature, the reaction was quenched with saturated aqueous ammonium chloride, and the aqueous layer was extracted with CH_2Cl_2 (3×30 mL). The combined organic layers were washed with brine, and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was purified through column chromatography on silica gel to give **6a** as a white solid (324.8 mg). Yield: 97%; The enantiomeric excess of 98% with the *R* isomer as the major product was determined by HPLC (Chiracel AD column, hexane/propan-2-ol 80:20; flow rate 1 mL min^{-1}; *R* isomer, t_R 7.05 min and *S* isomer, t_R 9.28 min).

***N*-[1-(4-Methoxyphenyl)propyl]-*P*,*P*-diphenylphosphinoylamide (6b)**: This compound was obtained as a white solid (32.5 mg) in 89% yield: $[\alpha]_D^{15} = +50.0$ ($c = 0.122$ in acetone); the enantiomeric excess of 97% with the *R* isomer as the major product was determined by HPLC (Chiracel AD column, hexane/propan-2-ol 80:20; flow rate 1 mL min^{-1}; *R* isomer, t_R 10.54 min and *S* isomer, t_R 13.15 min).

***N*-{1-[3,4-(Methylenedioxy)phenyl]propyl}-*P*,*P*-diphenylphosphinamide (6c)**: This compound was obtained as a white solid (34.7 mg) in 92% yield; $[\alpha]_D^{15} = +58.49$ ($c = 0.106$, acetone); the enantiomeric excess of 97% with the *R* isomer as the major product was determined by HPLC (Chiracel AD column, hexane/propan-2-ol 80:20; flow rate 1 mL min^{-1}; *R* isomer, t_R 8.32 min and *S* isomer, t_R 13.82 min)

***N*-[1-(4-Methylphenyl)propyl]-*P*,*P*-diphenylphosphinoylamide (6d)**: This compound was obtained as a white solid (33.3 mg) in 95% yield; $[\alpha]_D^{15} = +47.08$ ($c = 0.24$ in acetone); the enantiomeric excess of 98% with the *R* isomer as the major product was determined by HPLC (Chiracel AD column, hexane/propan-2-ol 92:8; flow rate 1 mL min^{-1}; *R* isomer, t_R 7.79 min and *S* isomer, t_R 9.44 min)

***N*-[1-(3-Methylphenyl)propyl]-*P*,*P*-diphenylphosphinamide (6e)**: This compound was obtained as a white solid (30.1 mg) in 86% yield; $[\alpha]_D^{15} = +21.43$ ($c = 0.154$ in acetone); the enantiomeric excess of 96% with the *R* isomer as the major product was determined by HPLC (Chiracel AD column, hexane/propan-2-ol = 90:10; flow rate 1 mL min^{-1}; *R* isomer, t_R 5.82 min and *S* isomer, t_R 9.59 min)

Enantioselective addition of dibutylzinc to *N*-diphenylphosphinoyl benzalimine (5a, 0.1 mmol) in the presence of 3c (0.1 mmol)

***N*-(1-Phenylpentyl)-*P*,*P*-diphenylphosphinoylamide (8a)**: This compound was obtained as a white solid in 67% yield; m.p. 165–166 °C; $[\alpha]_D^{15} = +24.74$ ($c = 0.19$ in acetone); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.80$ (t, $J = 6.8$ Hz, 3H), 1.07–1.1.24 (m, 4H), 1.83–2.07 (m, 2H), 4.15 (m, 1H), 7.14–7.49 (m, 10H), 7.75–7.88 ppm (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 13.8, 22.3, 28.1, 39.4, 55.8, 126.4, 126.9, 128.1, 128.3, 128.4, 130.9, 131.6, 131.7, 131.8, 132.2, 132.4, 132.5, 143.8$ ppm; IR (Nujol): $\tilde{\nu} = 3221$ (NH), 1183 (P=O) cm^{-1}; MS (EI): *m*/*z* (%): 363 $[M]^+$, 305 $[M-Bu]$, 216 $[Ph_2PONH]^+$, 201 $[Ph_2PO]^+$; elemental analysis calcd (%) for $C_{23}H_{26}NOP$: C 76.01, H 7.21, N, 3.85; found: C 75.71, H 7.27, N 3.99. The enantiomeric excess of 97% with the *R* isomer as the major product was determined by HPLC (Chiracel OD column, hexane/propan-2-ol 80:20; flow rate 1 mL min^{-1}; *R* isomer, t_R 3.583 min and *S* isomer, t_R 5.169 min).

***N*-[1-(4-Methoxyphenyl)pentyl]-*P*,*P*-diphenylphosphinoylamide (8b)**: This compound was obtained as a white solid in 50% yield; m.p. 135–136 °C; $[\alpha]_D^{15} = +40.00$ ($c = 0.02$ in acetone); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.80$ (t, $J = 6.6$ Hz, 3H), 1.07–1.21 (m, 4H), 1.78–2.0 (m, 2H), 3.32 (m, 1H), 3.80 (s, 3H), 4.06–4.11 (m, 1H), 6.81–7.47 (m, 10H), 7.73–7.87 ppm (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 13.8, 22.3, 28.2, 39.3, 55.1, 55.2, 113.7, 127.5, 128.1, 128.2, 128.4, 131.2, 131.5, 131.5, 131.6, 131.7, 131.8, 132.4, 132.5, 133.0, 134.1, 136.0, 158.4$ ppm; IR (Nujol): $\tilde{\nu} = 3128$(NH), 1189 (P=O) cm^{-1}; MS (EI): *m*/*z* (%): 394 $[M+1]^+$, 337 $[M+1-Bu]$, 336 $[M-Bu]$, 319 $[M-Bu-16\ [Ph_2PONH]^+$, 201 $[Ph_2PO]^+$, 192 $[M-O]^+$, 136 $[M+1-Ph_2PO-Bu]^+$; elemental analysis calcd (%) for $C_{24}H_{28}NO_2P$: C 73.26, H 7.17, N 3.56; found: C 73.29, H 7.23, N 3.38 . The enantiomeric excess of 95% with the *R* isomer as the major product was determined by HPLC (Chiracel OD column, hexane/propan-2-ol 80:20; flow rate 1 mL min^{-1}; *R* isomer, t_R 4.294 min and *S* isomer, t_R 5.534 min).

***N*-{1-[3,4-(Methylenedioxy)phenyl]pentyl}-*P*,*P*-diphenylphosphinamide (8c)**: This compound was obtained as a white solid in 57% yield; m.p. 159 °C; $[\alpha]_D^{15} = +42.50$ ($c = 0.12$ in acetone); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.80$ (t, $J = 6.0$ Hz, 3H), 1.09–1.43 (m, 5H), 1.71–2.00 (m, 2H), 3.17–3.29 (brs, 2H,), 4.06 (m, 1H), 6.55–6.70 (m, 3H), 7.27–7.87 ppm (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 13.8, 22.2, 28.2,$

39.4, 55.6, 100.8, 106.6, 107.9, 119.9, 127.6,128.4, 131.2, 131.6, 131.8, 132.4, 132.5, 132.9, 137.8, 146.3, 147.6 ppm; IR (Nujol): $\tilde{\nu}$ = 3157 (NH), 1249 (C-O-C), 1192 (P=O), 1042 (C-O-C) cm^{-1}; MS (EI): *m*/*z* (%): 201 (70) $[Ph_2PO]^+$, 206 (100) $[M+1-Ph_2PO]^+$, 350 (65) $[M-C_4H_9]$, 408 $[M+1]$; elemental analysis calcd (%) for $C_{24}H_{26}NO_3P$: C 70.75, H 6.43, N, 3.44; found: C 70.51, H 6.50, N 3.78 . The enantiomeric excess of 97% with the *R* isomer as the major product was determined by HPLC (Chiracel OD column, hexane/propan-2-ol 80:20; flow rate 1 mL min^{-1}; *R* isomer, t_R 4.801 min and *S* isomer, t_R 6.389 min).

***N*-[1-(4-Methylphenyl)pentyl]-*P*,*P*-diphenylphosphinoylamide (8d)**: This compound was obtained as a white solid in 63% yield; m.p. 146.0–146.3 °C; $[\alpha]_D^{15}$ = +31.82 (*c* = 0.132 in acetone); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.80 (t, *J* = 6.5 Hz, 3H), 1.02–1.1.25 (m, 4H), 1.83–1.96 (m, 2H), 2.35 (s, 1H), 4.09–4.14 (1H, m), 7.03–7.49 (10H, m), 7.76–7.90 ppm (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.8, 21.0, 22.3, 28.2, 39.2, 39.3, 55.6, 126.3, 128.1, 128.2, 128.4, 129.1, 131.1,131.6, 131.8, 132.3, 132.4, 132.6, 132.8, 136.5, 140.8 ppm; IR (Nujol): $\tilde{\nu}$ = 3137(NH), 1191 (P=O) cm^{-1}; MS (EI): *m*/*z* (%): 377 $[M]^+$, 376 $[M-1]$, 321 $[M+1-Bu]$, 320 $[M-Bu]$, 216 $[Ph_2PONH]^+$, 201 $[Ph_2PO]^+$, 176 $[M-Ph_2PO]^+$; elemental analysis calcd (%) for $C_{24}H_{28}NOP$: C 76.37, H 7.48, N, 3.71; found: C 76.11, H 7.34, N 3.62. The enantiomeric excess of 95% with the *R* isomer as the major product was determined by HPLC (Chiracel OD column, hexane/propan-2-ol 80:20; flow rate 1 mL min^{-1}; *R* isomer, t_R 3.627 min and *S* isomer, t_R 4.665 min).

***N*-[1-(3-Methylphenyl)pentyl]-*P*,*P*-diphenylphosphinoylamide (8e)**: This compound was obtained as a white solid in 55% yield; m.p. 149 °C; $[\alpha]_D^{15}$ = +21.43 (*c* = 0.154 in acetone); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.80 (t, *J* = 6.6 Hz, 3H), 1.08–1.23 (m, 4H), 1.81–1.97 (m, 2H), 2.31 (s, 3H), 4.09–4.11 (m, 1H), 6.90–7.48 (m, 10H), 7.73–7.87 ppm (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.8, 21.4, 22.3, 28.2, 39.3, 55.8, 123.3, 127.7, 127.7,128.0, 128.2, 128.4, 131.5, 131.7, 131.8, 132.5, 137.9, 143.7 ppm; IR (Nujol): $\tilde{\nu}$ = 3157(NH), 1250, 1193 (P=O) cm^{-1}; MS (EI): *m*/*z* (%): 377 $[M]^+$, 321 $[M+1-Bu]$, 320 $[M-Bu]$, 319 $[M-Bu-1]$, 216 $[Ph_2PONH]^+$, 201 $[Ph_2PO]^+$, 176 $[M-Ph_2PO]^+$; elemental analysis calcd (%) for $C_{24}H_{28}NOP$: C 76.37, H 7.48, N, 3.71; found: C 76.24, H 7.50, N 3.68. The enantiomeric excess of 95% with the *R* isomer as the major product was determined by HPLC (Chiracel OD column, hexane/propan-2-ol 80:20; flow rate 1 mL min^{-1}; *R* isomer, t_R 3.531 min and *S* isomer, t_R 4.604 min).

***N*-[1-(4-Bromophenyl)pentyl]-*P*,*P*-diphenylphosphinoylamide (8f)**: This compound was obtained as a white solid in 59% yield; $[\alpha]_D^{15}$ = +51.79 (*c* = 0.112 in acetone); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81 (t, *J* = 6.6 Hz, 3H), 1.06–1.1.26 (m, 4H), 1.75–1.94 (m, 2H), 3.21–3.25 (m, 1H), 4.09–4.14 (m, 1H), 7.01–7.47 (m, 10H), 7.74–7.87 ppm (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.8, 22.3, 28.1, 30.8, 39.2, 55.1, 120.6, 128.1, 128.2, 128.3, 128.4, 130.9, 131.4, 131.6, 131.8, 131.9, 132.3, 132.4, 132.7, 133.7, 142.9 ppm; IR (Nujol): $\tilde{\nu}$ = 3194 (NH), 1183 (P=O) cm^{-1}; HRMS calcd for $C_{23}H_{25}BrNOP$: 442.0930, found 442.0953. The enantiomeric excess of 96% with the *R* isomer as the major product was determined by HPLC (Chiracel OD column, hexane/propan-2-ol 80:20; flow rate 1 mL min^{-1}; *R* isomer, t_R 3.945 min and *S* isomer, t_R 5.134 min).

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