JOC Article

Evaluation of Chiral Oxazolines for the Highly Enantioselective Diethylzinc Addition to *N*-(Diphenylphosphinoyl) Imines†

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On the basis of the principle that the incorporation of the structurally rigid and conformationally restricted skeleton in β-amino alcohols is beneficial to the enantioselective diethylzinc addition to imines, a series of chiral oxazolines, which had been designed and conveniently prepared from commercially available (1*S*,2*S*)-2-amino-1-phenylpropane-1,3-diol, were applied in the diethylzinc addition to diphenylphosphinoyl imines to give high yields of 68−84% and excellent ee values of 90−95%. The configuration of the product was controlled by the chirality of the carbon bonded to the hydroxyl group in the oxazoline. Oxazolines bearing a *para*- or *meta*-substituted phenyl group generally offered higher enantioselectivity than those containing an *ortho*-substituted phenyl. The X-ray structures of **4f** and **4j**, in combination with the proposed transition state, preliminarily explained why oxazolines with a *para*- or *meta*-substituent on the phenyl group gave higher enantioselectivities than those bearing an *ortho*-substituent. This successful example using chiral oxazolines to promote the titled reaction implies that a large family of chiral compounds containing an oxazoline ring moiety have the potential to be developed for promoting the highly enantioselective dialkylzinc addition to *N*-(diphenylphosphinoyl) imines.

Introduction

The design of economical and efficient chiral ligands for highly enantioselective transformations has been one of the major projects in asymmetric synthesis.[1] Carbon−carbon bond-forming reactions are among the most useful methodologies for the construction of complex natural and unnatural molecules. Optically active amines are very important intermediates for the synthesis of some natural products, physiologically active substances, and pharmaceutical compounds.[2] Nevertheless, they are also extensively applied to the resolution of racemic compounds and asymmetric synthesis as chiral auxiliaries.[3] For all of these reasons, the development of efficient methods for approaching chiral amines has been receiving much attention. Other than the enantioselective reduction of prochiral imines and enamides,[4] the asymmetric addition of nucleophiles to imines is one of the most convenient methodologies for this purpose.[5] Highly enantioselective addition of diethylzinc to imines leading to optically active amines has been attracting increasing attention since the pioneer work reported by Soai in 1992, whose group used the ephedrine derivative (**1**) as a chiral ligand in the diethylzinc addition to *N*-(diphenylphosphinoyl) imines, leading to excellent enantioselectivity.[6a] Many chiral ligands have been designed for promoting this transformation, but most of them are limited to the derivatives of chiral amino alcohols.[6a−g,7] In particular, the conformationally restricted and structurally rigid artificial amino alcohols (**2**, **3**) generally exhibit higher

† This paper is dedicated to professor Zhi-Tang Huang at the Institute of Chemistry, Chinese Academy of Sciences, on the occasion of his 75th birthday.

‡ X.-M. Zhang and H.-L. Zhang contributed equally to this work.

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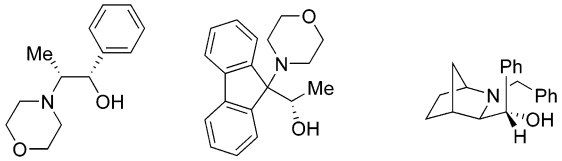
enantioselectivities than those induced by their simple and flexible analogues, but they suffer from the inconvenience associated with their multistep syntheses.[6e−f] Our continuous efforts have been devoted to evaluating easily accessible chiral ligands for highly enantioselective diethylzinc addition to imines, for example, fine-tuning the size of the substituents bonded to nitrogen has shown that a *N*-monosubstituted 1,2-diphenyl-2-aminoethanol efficiently promotes diethylzinc addition to imine with the high enantioselectivity of 98% ee.[7a] To find more efficient and easily prepared ligands for this addition, families of chiral ligands with a diversity of structures other than amino alcohols still need to be designed.



We envisioned that chiral oxazolines with a backbone similar to **1** had three structural characteristics that might enable them to be the promising candidates in competition with amino alcohols in promoting the diethylzinc addition of *N*-(diphenylphosphinoyl) imines. (1) They have sp^2-hybridized nitrogens, the conformations of which, restricted by the oxazoline ring, might make the structure of the ligand rigid, thereby minimizing the diastereomers formed in the transition state during catalysis. Such a transition state might be conductive to the chiral information of the carbon adjacent to hydroxyl group efficiently transmitting to the product. (2) The oxygen in the oxazoline ring is conjugated with C═N, which causes the nitrogen to be more Lewis basic, thus changing the Lewis acidity and catalytic activity of their zinc complexes. (3) The chiral environment could be systematically modified for the high enantioselectivity by fine-tuning the size of R groups in **4**. Our preliminary results on the use of chiral oxazolines in promoting diethylzinc addition to imines with high enantioselectivity have been presented previously.[6h] Herein, we would like to present our more extensive study on application of chiral oxazolines in the titled reaction.

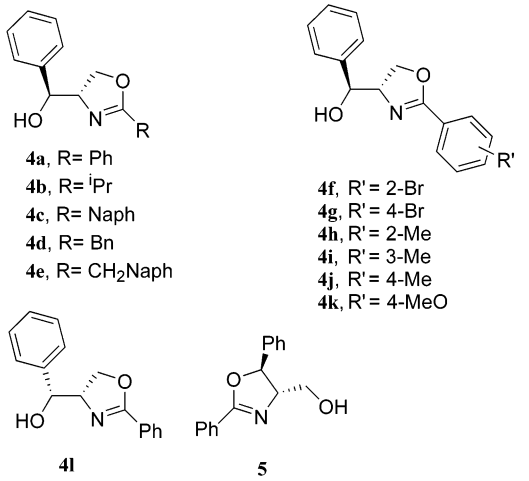
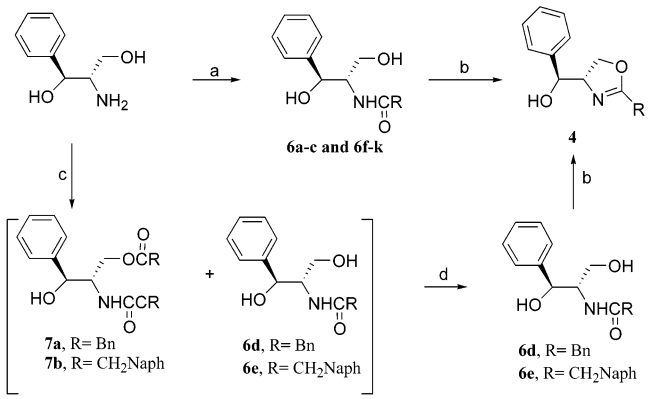


FIGURE 1. Chiral oxazolines used for present study.

SCHEME 1[a]



[a] Reagents and conditions: (a) RCOCl (1 equiv) or $(PhCO)_2O$ (for synthesis of **6a**, 1 equiv), Et_3N, THF, rt. (b) TsCl (1 equiv), Et_3N, CH_2Cl_2, reflux, 51−80%. (c) R^1CH_2COCl (2 equiv), $NaHCO_3$, H_2O, rt. (d) K_2CO_3, CH_3OH, rt, 54% (**6d**) and 71% (**6e**) (two steps).

Results and Discussion

Preparation of Oxazolines. The synthesis of the family of chiral oxazolines is very convenient, beginning with an amidition of (1*S*,2*S*)-2-amino-1-phenyl-propane-1,3-diol with RCOCl or $(RCO)_2O$ to provide amides **6a**−**k** according to the literature in high yields.[8] Among these compounds, **6b**, **6h**, **6i**, and **6k** were sufficiently pure for the next step without further purification (Scheme 1). Mixtures of over-acylation products **7a** and **7b** and the desired products **6d** and **6e** were observed when we followed a procedure similar to the synthesis of **6d** and **6e**. Partial hydrolysis of the mixture of **7a**, **7b**, **6d**, and **6e** in the presence of K_2CO_3 in methanol furnished the single products **6d** and **6e**. Compounds **6a**−**k** were treated with TsCl and Et_3N to provide the corresponding chiral oxazolines **4a**−**k** in good to high yields (Table 1).

High-quality crystals of **4f** and **4j** suitable for X-ray structural determination were obtained by slow evaporation from a mixture of CH_2Cl_2 and petroleum ether (see Supporting Information). It was found that the difference between oxazolines **4f** and **4j** existed in dihedral angles of the oxazoline ring and its conjugated substituted phenyl group. In oxazoline **4f**, the dihedral angle formed between oxazoline and *o*-bromophenyl is 42.45°, much larger than that formed between oxazoline and *p*-methylphenyl in oxazoline **4j** (18.62°). This means that an *ortho*-substitued phenyl group twists more out of conjugation with the oxazoline ring than a *para*- or *meta*-substituted phenyl group does, bringing subtle changes to the conformation of the transition state to influence the enantioselectivities and reaction rate. In line with the structural analysis for the oxazolines, we anticipate that oxazolines with an *ortho*-substitued phenyl group will have more influence on the enantioselectivity than those bearing a *para*- or *meta*-phenyl group.

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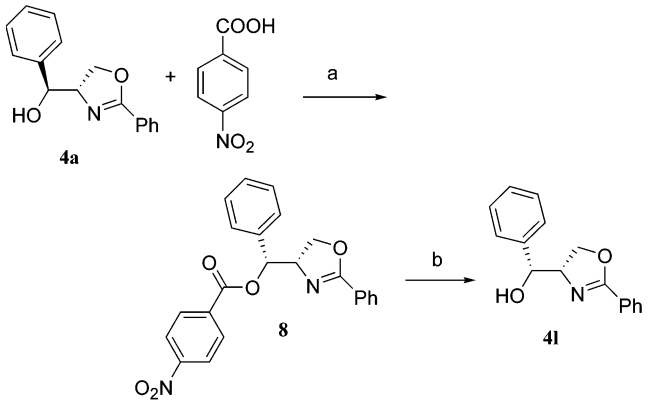
TABLE 1. Synthesis of Oxazolines 4a−k

amides **6**	R	yield (%)[a]	oxazoline **4**	yield (%)
6a	Ph	94	**4a**	80
6b	^{i}Pr	b	**4b**	80
6c	Naph	91	**4c**	63
6d	Bn	54	**4d**	51
6e	CH_2Naph	71	**4e**	51
6f	2-BrC_6H_4	86	**4f**	60
6g	4-BrC_6H_4	99	**4g**	65
6h	2-MeC_6H_4	b	**4h**	50
6i	3-MeC_6H_4	b	**4i**	53
6j	4-MeC_6H_4	96	**4j**	61
6k	4-$MeOC_6H_4$	b	**4k**	56

[a] Isolated yields for amides **6**. [b] Products were directly used in the next step without further purification.

SCHEME 2[a]



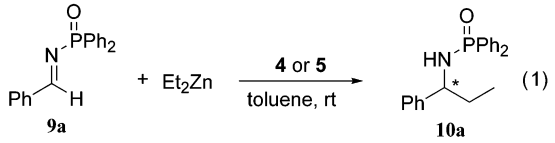
[a] Reagents and conditions: (a) Ph_3P, DEAD, THF, reflux, 21%. (b) K_2CO_3, CH_3OH, rt, 84%.

To clarify the influence of chirality of the carbon bonded to the hydroxy group, the oxazoline **4l** was prepared from **4a** by a Mitsunobu configuration inversion reaction sequence (Scheme 2).[9] The treatment of **4a** with PPh_3 and DEAD in refluxing THF gave **8** in 21% yield, which was directly subjected to a hydrolysis in the presence of K_2CO_3 to furnish **4l** in 84% yield (Scheme 2).

Ligand Survey. The different chiral oxazolines **4** and **5** were examined for the addition of diethylzinc to *N*-diphenylphosphinoyl benzalimine (**9a**) leading to *N*-(1-phenylpropyl)-diphenylphosphinoyl amide **10a** to find the optimal ligand. The nonpolar solvent toluene, which was found to maximize the rate difference between the catalyzed and the noncatalyzed reaction, was used as the reaction medium.[6b−e] The results of imine **9a** reacting with Et_2Zn in the presence of a stoichiometric amount of **4** and **5** in toluene at room temperature are summarized in Table 2.

It was found that this set of chiral oxazoline ligands were efficient and highly enantioselective for the titled reaction. High ee values of 81−93% were induced by most of the oxazolines **4a**−**k** (entries 1−11). The chiral carbon bonded to the hydroxyl group in the ligand was very important for getting high enantioselectivity. Without this chiral center, oxazoline **5** gave a very low ee value of 23% (entry 13). The configuration of the product was also controlled by the chiral carbon bonded to the

TABLE 2. Enantioselective Diethylzinc Addition of *N*-Diphenylphosphinoyl Benzalimine (9a) in the Presence of the Chiral Oxazolines 4 and 5[a]



entry	ligands	yield (%)[b]	ee (%)[c]	configuration[d]
1	**4a**	77	91	*S*
2	**4b**	62	85	*S*
3	**4c**	79	85	*S*
4	**4d**	70	87	*S*
5	**4e**	65	84	*S*
6	**4f**	35	81	*S*
7	**4g**	86	92	*S*
8	**4h**	77	84	*S*
9	**4i**	72	93	*S*
10	**4j**	89	91	*S*
11	**4k**	91	92	*S*
12	**4l**	56	76	*R*
13	**5**	55	23	*S*

[a] Reaction was carried out at room temperature in the presence of a stoichiometric amount of oxazoline for 48 h. [b] Isolated yield based on imine. [c] Determined on HPLC. [d] Determined by comparison of the retention time with literature values.[6]

hydroxyl group. When the configuration of this carbon was inverted, but that of the carbon bonded to the nitrogen in oxazoline ring maintained, as shown by **4a** and **4l**, the configuration of the product **10a** was inverted from *S* to *R* (entries 1 and 12); however, the enantioselectivity had a small decrease to 76% ee. Varying the size of the R group bonded to oxazoline ring resulted in a subtle change in the enantioselectivity (entries 1−5). It seemed that the enantioselectivity did not rely on the steric hindrance of the R group. Among **4a**−**e**, chiral oxazoline ligand **4a**, in which R was a phenyl group, showed the highest level of chiral induction for the diethylzinc addition to imine **9a**, giving an ee of 91%. On the basis of the X-ray structures of **4f** and **4j** (see Supporting Information), we expected that the R′ substituents bonded to the phenyl group at different positions might exhibit an obvious effect on the enantioselectivity. As we expected, the substituent at different positions on the phenyl in oxazoline exhibited a dramatic influence on the reaction (entries 6−11). In general, oxazolines bearing an *ortho*-substituted phenyl group would provide lower enantioselectivity than their analogues containing a phenyl group with *para* or *meta*-substituents. This might result from *ortho*-substituents causing the phenyl group to twist out of conjugation with the C=N double bond of oxazoline to form a distorted transition state upon coodination with diethylzinc, which is more unstable than that formed by oxazolines bearing *para*- *or meta*-substituted phenyl groups. The observation is also in agreement with our analysis. For example, oxazoline **4g**, having a *p*-bromophenyl group, promoted the diethylzinc addition to *N*-diphenylphosphinoyl benzalimine (**9a**), leading to a much higher enantioselectivity of 92% ee (entry 7) than that of 81% ee (entry 6) given by its analogue **4f**, which poccessed an *o*-bromophenyl group. Similar results were also observed with oxazolines **4h**−**j**. Compound **4i**, bearing a *m*-methylphenyl group, and **4j**, bearing a *p*-methylphenyl group, provided excellent enantioselectivities of 93 and 91% ee, respectively

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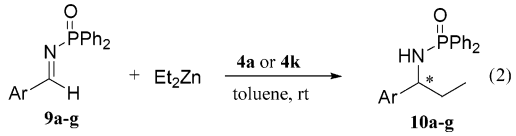
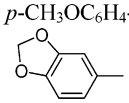
TABLE 3. Asymmetric Diethylzinc Addition to *N*-Diphenylphosphinoylimines 9a−g Promoted by the Ligand 4a and 4k



Entry	Ar	Ligand	Imine	Adduct	Yield (%)[a]	ee (%)[b]
1	C_6H_5-	**4a**	**9a**	**10a**	77	91
2		**4k**	**9a**	**10a**	72	93
3	*p*-ClC_6H_4-	**4a**	**9b**	**10b**	82	92
4	*p*-BrC_6H_4-	**4a**	**9c**	**10c**	83	90
5		**4k**	**9c**	**10c**	75	95
6	*p*-$CH_3OC_6H_4$-	**4a**	**9d**	**10d**	84	90
7		**4a**	**9e**	**10e**	75	90
8		**4k**	**9e**	**10e**	83	94
9	*p*-$CH_3C_6H_4$-	**4a**	**9f**	**10f**	72	93
10		**4k**	**9f**	**10f**	80	92
11	*m*-$CH_3C_6H_4$-	**4a**	**9g**	**10g**	68	93
12		**4k**	**9g**	**10g**	75	93

[a] Isolated yield. [b] Determined by HPLC analysis on a chiral column (Chiralcel OD or Chiralcel AD).

(entries 9 and 10), higher than that of 84% offered by **4h** containing an *o*-methylphenyl group (entry 8).

Enantioselective Diethylzinc Addition to Imines. Ligands **4a** and **4k** were extended to promote the diethylzinc addition to a range of diphenylphosphinoylimines. The corresponding results are recorded in Table 3. In the presence of ligand **4a**, ee values from 90 to 93% were obtained for all of the imine substrates tested. The substituents on the substrates did not exhibit any obvious effect on the enantioselectivity. Ligand **4k**, on average, gave slightly higher ee values of up to 95%, higher than the ee values of ligand **4a** for all of the substrates examined except for imine **9f**. Imine **9f** reacted with diethylzinc to provide chiral amide in 92% ee mediated by **4k**, a small amount lower than the ee value of 93% provided by **4a**.

By comparison of well-known ligands such as **1**−**3** for this transformation, we found that oxazoline **4k** exhibited higher enantioselectivity than **1** (up to 91% ee)[6a] and similar enantioselectivity as **2** (up to 95% ee),[6f] only a small amount lower than ligand **3** developed by Andersson and co-workers (98% ee).[6e] However, our ligand **4k** is much easier to prepare.

Reaction Mechanism. Andersson and co-workers proposed a transition state to explain the diethylzinc addition to imine on the basis of calculation.[6e] A structurally restricted chiral β-amino alcohol was evaluated on the basis of the transition state for diethylzinc addition to imine with high enantioselectivity. Our design of the oxazoline ligands was also based on the conclusion that conformationally restricted and structurally rigid artificial amino alcohols generally exhibited higher enantioselectivities than those induced by their simple and flexible analogues; therefore, we believed that the mechanism in our case should be similar to that proposed by Andersson and co-workers, as shown in Figure 2.[6e] This transition state accounted for the results we observed. As shown in structure **I**, products with *S* absolute configuration should be given by **4a**−**k**, which was consistent with the experimental results (Table 2, entries 1−11). The transition state, as demonstrated in **II**, clearly

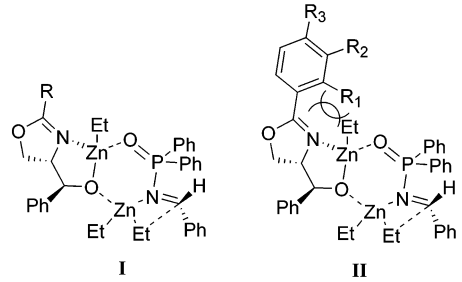


FIGURE 2. Proposed transition state for the titled reaction.

explained that the oxazoline containing an *ortho*-substituent on phenyl offered much greater effects on the enantioselectivity than that with a *para*- or *meta*-substituent. X-ray structures of **4f** and **4j** indicated that the repulsion brought about by the *ortho*-substituent on phenyl of oxazoline coordinated with zinc made the phenyl group twist out of conjugation with the oxazoline ring, which might form a much more unstable, that is, high-energy, transition state with a twisted conformation in comparison with the zinc complex of oxazoline with a *para*- or *meta*-substituted phenyl. Therefore, oxazolines with a *para*- or *meta*-substituent gave higher enantioselectivities than their structural analogues bearing an *ortho*-substituted phenyl group.

Conclusion

In conclusion, a series of chiral oxazolines were conveniently synthesized from commercial materials. Their application in activating diethylzinc addition to aromatic *N*-diphenylphosphinoylimines led to high yields and excellent ee values of 91−95%. The configuration of the product was controlled by the chirality of the carbon bonded to the hydroxyl group in the oxazoline. The X-ray structures of **4f** and **4j** combining with the proposed transition state explained that the oxazolines with a *para*- or *meta*-subsituent on the phenyl group gave higher

enantioselectivities than those bearing an *ortho*-substituent. This successful example using chiral oxazolines to promote the tilted reaction implied that a large family of chiral compounds containing an oxazoline ring moiety had the potential to be developed for promoting the highly enantioselective dialkylzinc addition to *N*-diphenylphosphinoylimines.

Experimental Section

General. All air- and moisture-sensitive reactions were carried out under a dry argon atmosphere using standard Schlenk line techniques. Toluene and THF were dried with sodium/benzophenone. CH_2Cl_2 was dried with CaH_2. Petroleum ether (PE) and ethyl acetate for column chromatography were distilled before use.

Materials. Commercial starting materials were used directly. The *N*-diphenylphosphinoylimines **9a**,[10−12,14] **9b**,[12−14] **9c**,[11,12,15] **9d**,[13,14] and **9f** [6a,16] were prepared according to the literature.[10−16] Ligand **5** was also prepared according to the literature.[8a]

***N*-Piperonylmethylidene-*P*,*P*-diphenylphosphinamide (9e).** This compound was prepared following a literature procedure[14] in 44% yield as a pale yellow solid: mp 154−155 °C; IR (Nujol; cm^{-1}) 1616, 1270, 1200; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 6.08−6.09 (m, 2H), 6.90−6.96 (m, 1H), 7.35−7.63 (m, 8H), 7.90−7.97 (m, 4H), 9.18 (d, J_{H-P} = 33.0 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 101.9, 106.8, 107.2, 108.3, 128.3, 128.4, 128.5, 128.6, 128.8, 130.7, 131.0, 131.4, 131.5, 131.6, 131.8, 132.3, 133.9, 148.5, 152.5, 171.8; MS (CI) *m/e* 349 (M^+), 272 (M − Ph), 202 (Ph_2POH^+), 201 (Ph_2PO^+). Anal. Calcd for $C_{20}H_{16}NO_3P$: C, 68.77; H, 4.62; N, 4.01. Found: C, 69.09; H, 4.74; N, 4.14.

***N*-(3-Methylphenylmethylidene)-*P*,*P*-diphenylphosphinamide (9g).** This compound was prepared following a literature procedure[14] in 54% yield as a pale yellow solid: mp 116−118 °C; IR (Nujol; cm^{-1}) 1628, 1200; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 2.45 (s, 3H), 7.40−7.51 (m, 8H), 7.69−7.97 (m, 6H), 9.30 (d, J_{H-P} = 33.0 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 21.2, 127.8, 128.3, 128.5, 128.7, 130.2, 131.4, 131.6, 131.7, 131.8, 132.1, 133.7, 134.5, 138.7, 173.8, 173.9; MS (CI) *m/e* 319 (M^+), 242 (M − Ph), 216 (Ph_2PONH^+), 202 (Ph_2POH^+), 201 (Ph_2PO^+). Anal. Calcd for $C_{20}H_{18}NOP$: C, 75.22; H, 5.68; N, 4.39. Found: C, 75.29; H, 5.53; N, 4.48.

Preparation and Characterization of (1*S*,2*S*)-2-Benzoylamino-1-phenyl-propane-1,3-diol (6a). To a solution of (1*S*,2*S*)-2-amino-1-phenyl-propane-1,3-diol (0.501 g, 3.0 mmol) in anhydrous THF (20 mL) were added Et_3N (5 mL) and benzoyl anhydride (0.678 g, 3.0 mmol). After the reaction mixture was stirred at room temperature for 16 h, the solvent was evaporated under the reduced pressure. The resulting residue was washed with water three times to give **6a** (0.765 g, 2.82 mmol, 94%) as a white solid: mp 192−195 °C; $[\alpha]_D$ +94.6 (*c* 1.0, EtOH); IR (Nujol; cm^{-1}) 3400, 3330, 3190, 1630; ^1H NMR (300 MHz, DMSO-d_6) δ (ppm) 3.37−3.42 (m, 1H), 4.17−4.19 (m, 1H), 4.75−4.79 (m, 1H), 4.93−4.96 (m, 1H), 5.51 (d, *J* = 5.4 Hz, 1H), 7.19−7.50 (m, 8H), 7.75−7.77 (m, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 57.5, 60.8, 70.7, 126.5, 127.1, 127.6, 128.1, 128.5, 131.4, 135.0, 143.9, 166.6; MS (CI) *m/e* 272 ($M + H^+$), 240 ($M - CH_2OH$), 222 ($M - CH_2OH - H_2O$), 164 (M − PhCHOH), 147 (M − PhCHOH − OH), 105 ($PhCO^+$). Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 70.63; H, 6.45; N, 5.08.

Preparation and Characterization of (1*S*,2*S*)-2-(1′-Naphthoylamino)-1-phenyl-propane-1,3-diol (6c). To a solution of (1*S*,2*S*)-2-amino-1-phenyl-propane-1,3-diol (0.334 g, 2.0 mmol) in anhydrous THF (20 mL) were added Et_3N (3 mL) and 1-naphthoyl chloride (0.381 g, 2.0 mmol). After the reaction mixture was stirred at room temperature for 16 h, the solvent was evaporated under reduced pressure. To the residue was added water (20 mL), and the resulting mixture was extracted with chloroform (3 × 20 mL). The combined organic layer was washed with 1 N HCl (20 mL) and dried over anhydrous Na_2SO_4. After removal of the solvent, the residue was recrystallized from a solvent mixture of PE, benzene, and ethyl acetate to give **6c** (0.587 g, 1.82 mmol, 91%) as white crystals: mp 144−145 °C; $[\alpha]_D$ +16.4 (*c* 1.0, EtOH); IR (Nujol; cm^{-1}) 3428, 3277, 1635; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 2.38−2.40 (br, 2H), 4.01−4.03 (m, 2H), 4.41−4.50 (m, 1H), 5.21 (d, *J* = 3.6 Hz, 1H), 6.57 (d, *J* = 1.4 Hz, 1H), 7.37−7.48 (m, 9H), 7.88−7.91 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 56.8, 64.0, 73.8, 124.6, 124.9, 125.2, 125.7, 126.3, 127.0, 127.8, 128.1, 129.7, 130.6, 133.4, 133.9, 141.0, 170.4; MS (CI) *m/e* 322 ($M + H^+$), 303 ($M - H_2O$), 285 ($M - 2H_2O$), 272 ($M - H_2O - CH_2OH$), 214 (M − PhCHOH), 197 (M − PhCHOH − OH), 155 ($NaphCO^+$). Anal. Calcd for $C_{20}H_{19}NO_3$: C, 74.75; H, 5.96; N, 4.36. Found: C, 74.37; H, 6.12; N, 4.34.

Preparation and Characterization of (1*S*,2*S*)-2-Phenylacetylamino-1-phenyl-propane-1,3-diol (6d). To a solution of (1*S*,2*S*)-2-amino-1-phenyl-propane-1,3-diol (1.67 g, 10.0 mmol) and $NaHCO_3$ (6.8 g, 80.0 mmol) in water (80 mL) was added phenylacetyl chloride (5 mL, 35 mmol) via an addition funnel for 0.5 h at room temperature. After being stirred for 8 h, the mixture was extracted with dichloromethane (3 × 50 mL). The combined organic layer was washed with brine and dried over Na_2SO_4. After removal of the solvent, to the resulting residue were added K_2CO_3 (3.0 g, 22 mmol) and methanol (300 mL). The mixture was stirred at room temperature for 12 h, and then the methanol was evaporated. To the residue was added water (100 mL), and the mixture was extracted with dichloromethane (3 × 50 mL). The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure, the residue was purified through column chromatography on silica gel to provide **6d** (1.537 g, 5.4 mmol, 54%) as white crystals: mp 97−100 °C; $[\alpha]_D$ +64.3 (*c* 1.0, $CHCl_3$); IR (Nujol; cm^{-1}) 3420, 3385, 3329, 3231, 1658; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 3.48 (d, *J* = 1.8 Hz, 2H), 3.75−3.78 (m, 2H), 4.02−4.04 (m, 1H), 4.99 (d, *J* = 3.4 Hz, 1H), 6.19 (d, *J* = 7.7 Hz, 1H), 7.10−7.18 (m, 2H), 7.27−7.34 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 43.3, 56.6, 62.8, 72.5, 125.6, 127.2, 127.5, 128.2, 128.8, 129.2, 134.3, 141.0, 172.3; MS(CI) 267 ($M - H_2O$), 236 ($M - H_2O - CH_2OH$), 178 (M − PhCHOH), 161 ($PhCH_2CONHCH-CH_2^+$), 107 ($PhCHOH^+$), 91 ($PhCH_2^+$). Anal. Calcd for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.71; N, 4.91. Found: C, 71.27; H, 6.80; N, 5.11.

Preparation of (1*S*,2*S*)-2-(1-Naphthylacetylamino)-1-phenyl-propane-1,3-diol (6e). To a solution of (1*S*,2*S*)-2-amino-1-phenyl-propanediol (0.334 g, 2 mmol) and $NaHCO_3$ (1.0 g, 12.0 mmol) in water (20 mL) was added a solution of 1-naphthylacetyl chloride (0.818 g, 4 mmol) in dichloromethane (5 mL) via an addition funnel at room temperature. After being stirred for 50 h, the mixture was extracted with dichloromethane (3 × 20 mL). The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. After removal of the solvent, to the resulting residue were added K_2CO_3 (1.0 g, 7.1 mmol) and methanol (50 mL). The mixture was stirred at room temperature for 18 h, then the methanol was evaporated. To the residue was added water (20 mL), and the mixture was extracted with dichloromethane (3 × 20 mL). The combined organic layer was washed with 1 N HCl and brine and dried over anhydrous Na_2SO_4. The solvent was removed to provide **6e** (0.474 g, 1.42 mmol, 71%) as a white

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solid. The crude product was used in the following reaction without purification.

Preparation of (1*S*,2*S*)-2-(2′-Bromobenzoylamino)-1-phenyl-propane-1,3-diol (6f). To a solution of (1*S*,2*S*)-2-amino-1-phenyl-propanediol (836 mg, 5 mmol) in dichloromethane (30 mL) and anhydrous triethylamine (10 mL) was added 2-bromobenzoyl chloride (1097 mg, 5 mmol). After the reaction mixture was stirred at room temperature for 8 h, evaporation of the solvent under reduced pressure provided a white solid. Washing the solid with water and drying gave **6f** (1.51 g) in 86% yield: mp 135−136 °C; IR (Nujol; cm^{-1}) 3400, 3330, 3190, 1630; ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 3.36−3.41 (m, 1H), 3.59−3.67 (m, 1H), 4.09−4.15 (m, 1H), 4.82−4.86 (m, 1H), 4.94−4.97 (m, 1H), 5.41 (d, J = 5.7 Hz, 1H), 7.15−7.40 (m, 8H), 7.58 (d, J = 7.8 Hz, 1H), 7.89 (d, J = 8.7 Hz, 1H); ^{13}C NMR (300 MHz, DMSO-d_6) δ (ppm) 57.2, 60.6, 70.2, 119.2, 126.6, 127.1, 127.7, 128.1, 129.1, 131.1, 133.0, 139.4, 143.7, 167.3; MS (CI) *m/e* 77, 91, 118, 146, 155, 157, 183 (^{79}BrPhCO$^+$, 100%), 185 (^{81}BrPhCO$^+$, 100%), 225, 227, 242 (M − PhCHOH − 1), 244. Anal. Calcd for $C_{16}H_{16}BrNO_3$: C, 54.87; H, 4.60; N, 4.00. Found: C, 54.51; H, 4.64; N, 3.79.

Preparation of (1*S*,2*S*)-2-(4′-Bromobenzoylamino)-1-phenyl-propane-1,3-diol (6g). To a solution of (1*S*,2*S*)-2-amino-1-phenyl-propanediol (501 mg, 3.0 mmol) in THF (25 mL) and anhydrous triethylamine (10 mL) was added 4-bromobenzoyl chloride (658 mg, 3 mmol). After the reaction mixture was stirred at room temperature for 2 h, removal of the solvent under reduced pressure provided a white solid. Washing the solid with water and drying gave **6g** (1.04 g) in 99% yield: mp 213−215 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 3.54−3.61 (m, 2H), 4.13−4.17 (m, 1H), 4.75−4.79 (m, 1H), 4.89−4.91 (m, 1H), 5.48−5.50 (d, J = 5.1 Hz, 1H), 7.15−7.34 (m, 5H), 7.62−7.72 (m, 4H), 7.92 (d, J = 8.7 Hz, 1H); ^{13}C NMR (300 MHz, DMSO-d_6) δ (ppm) 57.7, 60.8, 70.9, 125.1, 126.6, 127.1, 128.1, 129.8, 131.5, 134.1, 143.8, 165.8; MS (CI) *m/e* 183 (^{79}BrPhCO$^+$, 100%), 185 (^{81}BrPhCO$^+$, 100%), 225, 227, 242 (M − PhCHOH − 1), 244, 350 (M + 1), 352 (M + 1). Anal. Calcd for $C_{16}H_{16}BrNO_3$: C, 54.87; H, 4.60; N, 4.00. Found: C, 54.74; H, 4.58; N, 4.00.

Preparation of (1*S*,2*S*)-2-(4′-Methylbenzoylamino)-1-phenyl-propane-1,3-diol (6j). To a solution of (1*S*,2*S*)-2-amino-1-phenyl-propanediol (501 mg, 3.0 mmol) in THF (25 mL) and anhydrous triethylamine (10 mL) was added 4-methylbenzoyl chloride (464 mg, 3.0 mmol). After the reaction mixture was stirred at room temperature for 2 h, removal of the solvent under reduced pressure provided a white solid. Washing the solid with water and drying gave **6j** (824 mg) in 96% yield: mp 201−202 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ (ppm) 2.33 (s, 3H, CH_3), 3.34−3.39 (m, 1H), 3.56−3.64 (m, 1H), 4.15−4.18 (m, 1H), 4.75−4.79 (m, 1H), 4.92−4.95 (d, J = 5.4 Hz, 1H), 7.16−7.35 (m, 7H), 7.66 (d, J = 7.8 Hz, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm) 21.3, 57.5, 60.8, 70.7, 126.5, 127.1, 127.6, 128.1, 129.1, 132.2, 141.2, 143.9, 166.5; MS (CI) 119, 161 (100%), 178 (M − PhCHOH, 31%), 286 (M + 1). Anal. Calcd for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.71; N, 4.91. Found: C, 71.30; H, 6.76; N, 5.08.

Preparation and Characterization of [(*S*,*S*)-2-Phenyl-4,5-dihydro-oxazole-4-yl]-phenyl-methanol (4a). To a solution of **6a** (1.626 g, 6.0 mmol) in anhydrous dichloromethane (30 mL) and Et_3N (30 mL) was added *p*-toluenesulfonyl chloride (1.261 g, 6.0 mmol). After the reaction mixture was refluxed for 24 h, the solvent was evaporated. To the residue was added water (50 mL), and the aqueous layer was extracted with dichloromethane (3 × 30 mL). The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. After removal of the solvent, the residue was purified through column chromatography on silica gel (eluent: PE/ethyl acetate/Et_3N = 3/1/1) to give **4a** (1.221 g, 4.8 mmol, 80%) as a white solid: mp 94−97 °C; $[\alpha]_D$ +77.7 (*c* 1.0, $CHCl_3$); IR (Nujol, cm^{-1}) 3390, 1643; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 3.50 (br, 1H), 4.12−4.19 (m, 1H), 4.26−4.32 (m, 1H), 4.56−4.60 (m, 2H), 7.28−7.46 (m, 8H), 7.98−8.01 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 69.4, 73.0, 76.5, 127.0, 127.2, 128.2, 128.3, 128.4, 128.5, 131.6, 140.0, 165.3; MS(CI) 254 (M + H^+), 236 (M − OH), 147 (M + H − PhCHOH), 105 ($PhCO^+$). Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 76.00; H, 5.93; N, 5.43.

Other analogues of **4a**, except **4b**, were prepared in a manner similar to that described above and on the same reaction scale (6 mmol scale).

[(*S*,*S*)-2-(1′-Naphthyl)-4,5-dihydro-oxazole-4-yl]-phenyl-methanol (4c). The crude product was purified through column chromatography on silica gel (eluent: PE/ethyl acetate/Et_3N = 3/1/1) to give **4c** (63%) as a colorless oil: $[\alpha]_D$ +27.4 (*c* 1.0, $CHCl_3$); IR (Nujol; cm^{-1}) 3350, 1641; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 3.44 (br, 1H), 4.18−4.24 (m, 1H), 4.29−4.35 (m, 1H), 4.68−4.76 (m, 2H), 7.38−7.63 (m, 9H), 7.88−8.12 (m, 3H), 9.14 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 68.5, 73.5, 76.9, 124. 2, 124.6, 126.2, 126.3, 127.1, 127.3, 128.1, 128.3, 128.5, 129.2, 131.0, 132.2, 133.7, 140.1, 165.4; MS(CI): 304 (M + H^+), 272 (M − OH − N), 255 (M − H_2O − CH_2O), 196 (M − PhCHOH), 155 ($C_{10}H_7CO^+$), 107 ($PhCHOH^+$); HRMS calcd for $C_{20}H_{17}NO_2$ 303.1259, found 303.1263.

[(*S*,*S*)-2-Benzyl-4,5-dihydro-oxazole-4-yl]-phenyl-methanol (4d). The residue was recrystallized from a solvent mixture of PE and ethyl acetate to give **4d** (51%) as white crystals: mp 116−119 °C; $[\alpha]_D$ +76.0 (*c* 1.0, $CHCl_3$); IR (Nujol, cm^{-1}) 3220, 1660; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 3.38 (br, 1H) 3.66 (s, 2H), 3.97−4.03 (m, 1H), 4.08−4.14 (m, 1H), 4.37−4.45 (m, 1H), 4.53 (d, J = 7.8 Hz, 1H), 7.18−7.39 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 34.7, 69.4, 72.3, 76.6, 127.0, 128.1, 128.5, 128.6, 128.8, 128.9, 129.3, 134.7, 139.9, 168.0; MS (CI) 267 (M^+), 161 (M − PhCHOH), 118 ($PhCH_2$-CNH^+), 91 ($PhCH_2^+$). Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.07; H, 6.48; N, 5.24.

[(*S*,*S*)-2-Naphthylmethyl-4,5-dihydro-oxazole-4-yl]-phenyl-methanol (4e). The residue was purified through column chromatography on silica gel (eluent: PE/ethyl acetate/Et_3N = 2/1/1) to give **4e** (51%) as white crystals: mp 111−114 °C; $[\alpha]_D$ +60.7 (*c* 1.0, $CHCl_3$); IR (Nujol) cm^{-1} 3250, 1644; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 3.93−3.99 (m, 1H), 4.04−4.10 (m, 3H), 4.35−4.43 (m, 1H), 4.48 (d, J = 7.8 Hz, 1H), 7.28−7.56 (m, 9H), 7.79−7.89 (m, 2H), 8.12−8.15 (d, J = 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 32.5, 69.5, 72.4, 76.5, 123.8, 125.4, 125.8, 126.3, 126.9, 127.5, 128.0, 128.1, 128.4, 128.7, 131.0, 132.0, 133.8, 139.9, 168.0; MS (CI) 317 (M^+), 299 (M − H_2O), 211 (M + H − PhCHOH), 141 ($NaphCH_2^+$). Anal. Calcd for $C_{21}H_{19}NO_2$: C, 79.47; H, 6.03; N, 4.41. Found: C, 79.25; H, 6.17; N, 4.41.

[(*S*,*S*)-2-(2′-Bromophenyl-4,5-dihydro-oxazole-4-yl)-phenyl-methanol (4f): yield 60%; mp 79.3−81.9 °C; $[\alpha]^{25}_D$ +70.6 (*c* 1.0, $CDCl_3$); IR (Nujol) cm^{-1} 3390 (OH), 1643 (C=N); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 2.7 (br, 1H), 4.23−4.38 (m, 2H), 4.61−4.71 (m, 2H), 7.28−7.49 (m, 7H), 7.67−7.73 (m, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ (ppm) 69.5, 72.9, 76.5, 121.9, 127.0, 127.1, 128.2, 128.5, 129.2, 131.2, 131.8, 133.8, 139.9, 164.7; MS(CI) 77, 79, 107, 146, 183 (^{79}BrPhCO$^+$, 100%), 185 (^{81}BrPhCO$^+$, 100%), 225 (M + 1 − PhCHOH, 59%), 227 (M + 1 − PhCHOH, 60%), 332 (M + H^+), 334 (M + H^+). Anal. Calcd for $C_{16}H_{14}BrNO_2$: C, 57.85; H, 4.25; N, 4.22. Found: C, 57.63; H, 4.46; N, 4.41.

Crystal Data: $C_{16}H_{14}BrNO_2$, MW = 332.19, monoclinic, space group $P2_1$, a = 12.624(2), b = 8.817(2), c = 14.573(2) Å, α = 90°, β = 113.26(1)°, γ = 90°, U = 1490.2(5) Å^3, T = 295(2) K, Z = 4, D_c = 1.481 mg/m^3, μ = 2.759 mm^{-1}, λ = 0.71073 Å, F(000) 672, crystal size 0.48 × 0.48 × 0.44 mm, 4711 reflections collected, 4064 independent reflection [R_{int} = 0.0159]; refinement method, full-matrix least-squares on F^2; goodness-of-fit on F^2 = 0.879, final R indices [$I > 2\sigma(I)$] R_1 = 0.0362, wR_2 = 0.0669.

[(*S*,*S*)-2-(4′-Bromophenyl-4,5-dihydro-oxazole-4-yl)-phenyl-methanol (4g): yield 65%; mp 150.4−152.4 °C; $[\alpha]^{25}_D$ +49.8 (*c* 1.0, $CDCl_3$); IR (Nujol) cm^{-1} 3200, 1640; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 3.50 (br, 1H), 4.15−4.27 (m, 2H), 4.54−

4.58 (m, 2H), 7.28−7.46 (m, 5H), 7.54−7.57 (d, J = 8.4 Hz, 2H), 7.82−7.85 (d, J = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 69.5, 73.0, 76.5, 127.0, 128.2, 128.5, 129.9, 131.6, 139.9, 164.5; MS (CI) 77, 79, 107, 146, 183 (^{79}BrPhCO$^+$, 100%), 185 (^{81}BrPhCO$^+$, 100%), 224 (M − PhCHOH, 54%), 225 (M + 1 − PhCHOH, 96%), 226 (M − PhCHOH, 62%), 227 (M + 1 − PhCHOH, 93%), 332 (M + H$^+$), 334 (M + H$^+$). Anal. Calcd for $C_{16}H_{14}BrNO_2$: C, 57.85; H, 4.25; N, 4.22. Found: C, 57.61; H, 4.50; N, 4.35.

[(*S*,*S*)-2-(2′-Methylphenyl-4,5-dihydro-oxazole-4-yl)-phenyl-methanol (4h): yield 50%; $[\alpha]^{25}_D$ +52.7 (*c* 0.8, $CDCl_3$); IR (Nujol) cm^{-1} 3242−3374, 1643; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 2.60 (s, 3H), 3.93 (br, 1H), 4.11−4.25 (m, 2H), 4.59−4.63 (m, 2H), 7.23−7.47 (m, 7H), 7.83(d, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 21.7, 68.6, 73.2, 125.6, 126.8, 127.1, 128.1, 128.2, 128.4, 129.9, 130.8, 131.2, 138.8, 140.1, 165.9; MS (CI) 119 (PhCH(OH)C$^+$, 100%); 160 (M − PhCHOH, 90%); 161 (M + 1 − PhCHOH, 75%), 268 (M + H$^+$). Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.34; H, 6.44; N, 5.36.

[(*S*,*S*)-2-(3′-Methylphenyl-4,5-dihydro-oxazole-4-yl)-phenyl-methanol (4i): yield 53%; $[\alpha]^{25}_D$ +83.1 (*c* 0.6, $CDCl_3$); IR (Nujol) cm^{-1} 3250−3351, 1644; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 2.34 (s, 3H), 4.10−4.23 (m, 2H), 4.57−4.65 (m, 2H), 4.80 (br, 1H), 7.24−7.47 (m, 7H), 7.77−7.84 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 21.1, 69.3, 72.9, 125.5,127.1, 127.2, 127.9, 128,2, 128.4, 129.0, 132.3, 137.9, 140.0, 165.5; MS (CI) 119 (PhCH(OH)C$^+$, 88%); 160 (M − PhCHOH, 76%); 161 (M + 1 − PhCHOH, 100%), 268 (M + H$^+$). Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.06; H, 6.60; N, 5.31.

[(*S*,*S*)-2-(4′-Methylphenyl-4,5-dihydro-oxazole-4-yl)-phenyl-methanol (4j): yield 61%; mp 105.8−106.7 °C; $[\alpha]^{25}_D$ +67.5 (*c* 1.0, $CDCl_3$); IR (Nujol) cm^{-1} 3189, 1642; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 2.41 (s, 3H), 4.10−4.26 (m, 2H), 4.51−4.60 (m, 2H), 7.20−7.44 (m, 7H), 7.87 (d, J = 8.1 Hz, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ (ppm) 21.5, 69.3, 72.9, 76.6, 124.4, 127.0, 128.1, 128.3, 128.5, 129.0, 140.2, 142.0, 165.4; MS(CI) 91, 105 (PhCO$^+$), 119, 132, 160 (M − PhCHOH, 100%), 161, 250 (M − OH), 268 (M + H$^+$). Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N 5.24. Found: C, 76.16, H 6.42, N 5.40.

Crystal Data: $C_{17}H_{17}NO_2$, MW = 267.32, Monoclinic, space group $P2_1$, a = 7.778(2), b = 9.602(3), c = 9.977(2) Å, α = 90°, β = 97.20(2)°, γ = 90°, U = 739.3(3) Å^3, T = 295(2) K, Z = 2, D_c = 1.201 mg/m^3, μ = 0.079 mm^{-1}, λ = 0.71073 Å, F(000) 284, crystal size 0.58 × 0.44 × 0.20 mm, 1996 reflections collected, 1798 independent reflection [R_{int} = 0.0113]; refinement method, full-matrix least-squares on F^2; goodness-of-fit on F^2 = 0.831, final R indices [$I > 2\sigma(I)$] R_1 = 0.0376, wR_2 = 0.0746.

[(*S*,*S*)-2-(4′-Methoxylphenyl-4,5-dihydro-oxazole-4-yl)-phenyl-methanol (4k): yield 56%; mp 85.5−86.2 °C; $[\alpha]^{25}_D$ +51.0 (*c* 1.0, $CDCl_3$); IR (Nujol) cm^{-1} 3192, 1638; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 3.50 (br, 1H), 3.87 (s, 3H), 4.12−4.29 (m, 2H), 4.52−4.59 (m, 2H), 6.93 (d, J = 7.8 Hz, 2H), 7.27−7.47 (m, 5H), 7.94 (d, J = 7.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 55.2, 69.3, 72.8, 113.6, 119.6, 127.0, 128.0, 128.4, 130.1, 140.3, 162.2, 165.1; MS (CI) 177 (M + 1 − PhCHOH, 100%), 284 (M + H$^+$). Anal. Calcd for $C_{17}H_{17}NO_3$: C, 72.07; H, 6.05; N, 4.94. Found: C, 71.84; H, 6.12; N, 5.21.

Preparation and Characterization of [(*R*,*S*)-2-Phenyl-4,5-dihydro-oxazole-4-yl]-phenyl-methanol (4l). To a solution of triphenylphosphine (314 mg, 1.2 mmol), 4-nitrobenzoic acid (200 mg, 1.2 mmol), and DEAD (209 mg, 1.2 mmol) in THF (5 mL) was added a solution of [(*S*,*S*)-2-phenyl-4,5-dihydro-oxazole-4-yl]-phenyl-methanol **4a** (253 mg, 1.0 mmol) in THF (5 mL) dropwise. After the reaction mixture was refluxed for 10 h, removal of the solvent and purification of the residue through a column chromatography (eluent: EtOAc/PE = 1/4) gave **8** in 21% yield as a colorless oil. Intermediate **8** was dissolved in the solution of K_2CO_3 in CH_3OH and stirred overnignt at room temperature. After removal of the solvent, the residue was purified through column chromatography (eluent: EtOAc/PE = 1/3) to give **4l** (44 mg) as white crystals: yield 84%; mp 163−165 °C; $[\alpha]^{25}_D$ −28.9 (*c* 10.5, $CHCl_3$); IR (Nujol) cm^{-1} 3390 (OH), 1643 (C=N); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 3.13−3.21 (br, 1H), 4.16−4.22 (m, 1H), 4.44−4.49 (m, 1H), 4.64−4.71 (m, 1H), 5.32 (d, J = 2.8 Hz, 1H), 7.29−7.53 (m, 8H), 7.92−7.95 (m, 2H); ^{13}C NMR (75 MHz, $CHCl_3$) δ (ppm) 67.1, 72.2, 72.6, 125.6, 125.9, 126.9, 127.3, 127.5, 128.1, 128.2, 128.3, 128.4, 128.6, 131.4, 140.4, 166.0; MS(CI) 254 (M + H$^+$), 236 (M − OH), 147 (M + H − PhCHOH), 105 (PhCO$^+$); HRMS calcd for $[C_{16}H_{13}NO]^+$ 235.0997, found 235.0996.

[(*S*,*S*)-2-Isopropyl-4,5-dihydro-oxazole-4-yl]-phenyl-methanol (4b). To a solution of (1*S*,2*S*)-2-amino-1-phenyl-propanediol (0.167 g, 1.0 mmol) in anhydrous THF (10 mL) were added Et_3N (1.5 mL) and isobutylryl chloride (0.678 g, 3.0 mmol). After the reaction mixture was stirred at room temperature for 16 h, the solvent was evaporated under reduced pressure. The residue was dissolved in anhydrous dichloromethane (10 mL) and Et_3N (10 mL). To the solution was added *p*-toluenesulfonyl chloride (0.191 g, 1 mmol). After the reaction mixture was refluxed for 24 h, the solvent was evaporated. To the residue was added water (20 mL), and the aqueous layer was extracted with dichloromethane (3 × 10 mL). The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. After removal of the solvent, the residue was purified through column chromatography on silica gel (eluent: PE/ethyl acetate/Et_3N = 4/1/1) to give **4b** (0.176 g, 0.8 mmol, 80%) as white crystals: mp 65−68 °C; $[\alpha]^{25}_D$ +89.7 (*c* 1.0, $CHCl_3$); IR (Nujol) cm^{-1} 3175, 1652; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 1.18−1.21 (m, 6H), 2.55−2.64 (m, 1H), 3.96−4.01 (m, 1H), 4.05−4.11 (m, 1H), 4.31−4.39 (m, 1H), 4.49 (d, J = 7.8 Hz, 1H), 7.28−7.43 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 19.6, 28.1, 68.9, 72.1, 76.5, 127.0, 128.1, 128.4, 139.9, 173.7; MS (CI) 220 (M + H$^+$), 113 (M − PhCHOH), 43 (^{i}Pr$^+$); HRMS calcd for $C_{13}H_{17}NO_2$ 219.1259, found 219.1252.

General Procedure for the Enantioselective Addition of Diethylzinc to *N*-(Diphenylphosphinoyl) Imines. *N*-(Diphenylphosphinoyl) benzalimine (**9a**) (30.5 mg, 0.1 mmol) and oxazoline **4a** (25.3 mg, 0.1 mmol) were dissolved in dry toluene (1.5 mL) under argon. To the mixture was added Et_2-Zn in hexane (1 M, 0.5 mL, 0.5 mmol) at room temperature. After the mixture was 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 layer was 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 *N*-(1-phenylpropyl)-*P*,*P*-diphenylphosphinoylamide (**10a**) (25.8 mg, 0.077 mmol, 77%) as a white solid: mp 155−157 °C; IR (Nujol) cm^{-1} 3135, 1188; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 0.80 (t, J = 7.4 Hz, 3H), 1.80−1.95 (m, 1H), 1.98−2.10 (m, 1H), 3.32 (m, 1H), 4.10 (m, 1H), 7.15−7.46 (m, 11H), 7.78−7.89 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 10.5, 32.5, 57.1, 125.0, 126.4, 126.6, 127.0, 128.1, 128.3, 128.4, 128.5, 131.6, 131.7, 131.8, 132.4, 132.6, 143.4; MS (CI) 334 (M − H), 306 (M − CH_2CH_3), 258 (M − Ph), 216 (Ph_2PONH^+), 201 (Ph_2PO^+). The (*S*)-isomer (major product) was obtained in 91% ee as determined by HPLC (Chiracel AD column, hexane/propan-2-ol = 80/20; flow rate = 1 mL/min; (*R*)-isomer, t_R = 13.17 min; (*S*)-isomer, t_R = 17.82 min).

***N*-[1-(4′-Chlorophenyl)propyl]-*P*,*P*-diphenylphosphinoylamide (10b).** This compound (30.3 mg, 0.082 mmol, 82%) was obtained as a white solid: mp 184−185 °C; IR (Nujol) cm^{-1} 3220, 1184; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 0.80 (t, J = 7.4 Hz, 3H), 1.82 (m, 1H), 1.98 (m, 1H), 3.36 (m, 1H), 4.07 (m, 1H), 7.08−7.48 (m, 10H), 7.70−7.90 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 10.5, 32.3, 56.4, 127.9, 128.1, 128.2, 128.3, 128.4, 128.5, 128.7, 131.7, 131.8, 132.0, 132.3, 132.4, 132.6, 132.7, 133.7, 142.0, 142.1; MS (CI) 369 (M$^+$), 341 (M − CH_2=CH_2), 259 (M + H − ClC_6H_4), 217 ($Ph_2PONH_2^+$), 202 (Ph_2POH^+). Anal. Calcd for $C_{21}H_{21}ClNOP$: C, 68.20; H, 5.72; N, 3.79; Cl, 9.59. Found: C, 68.29; H, 5.75; N, 3.69; Cl, 9.40.

The (*S*)-isomer (major product) was obtained in 92% ee as determined by HPLC (Chiracel AD column, hexane/propan-2-ol = 95/5; flow rate = 1 mL/min; (*R*)-isomer, t_R = 9.87 min and (*S*)-isomer, t_R = 11.15 min).

***N*-[1-(4-Bromophenyl)propyl]-*P,P*-diphenylphosphinoylamide (10c).** This compound (34.4 mg, 0.083 mmol, 83%) was obtained as a white solid: mp 174−176 °C; IR (Nujol) cm^{-1} 3224, 1184; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 0.78 (t, J = 7.2 Hz, 3H), 1.74−1.84 (m, 1H), 1.86−2.01 (m, 1H), 3.38 (m, 1H), 4.05 (m, 1H), 7.03 (d, 2H, J = 7.8 Hz), 7.27−7.48 (m, 8H), 7.70−7.74 (m, 2H), 7.83−7.89 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 10.5, 32.3, 56.5, 120.7, 128.2, 128.3, 128.5, 130.8, 131.4, 131.7, 131.8, 132.3, 132.4, 132.5, 133.5, 142.5, 142.6; MS (CI) 415 (M^+), 385 (M − CH_2=CH_2), 305 (M − Br − CH_2CH_3), 212 (M − Ph_2PO), 201 (Ph_2PO^+). Anal. Calcd for $C_{21}H_{21}BrNOP$: C, 60.88; H, 5.11; N, 3.38; Br, 19.29. Found: C, 60.97; H, 5.16; N, 3.53; Br, 19.15. The (*S*)-isomer (major product) was obtained in 90% ee as determined by HPLC (Chiracel AD column, hexane/propan-2-ol = 80/20; flow rate = 1 mL/min; (*R*)-isomer, t_R = 11.12 min; (*S*)-isomer, t_R = 12.82 min).

***N*-[1-(4-Methoxyphenyl)propyl]-*P,P*-diphenylphosphinoylamide (10d).** This compound (30.7 mg, 0.084 mmol, 84%) was obtained as a white solid: mp 173−174 °C; IR (Nujol) cm^{-1} 3203, 1182; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 0.78 (t, J = 7.4 Hz, 3H), 1.77−1.86 (m, 1H), 1.96−2.05 (m, 1H), 3.31 (m, 1H), 3.81 (s, 3H), 4.04−4.07 (m, 1H), 6.83 (d, J = 8.7 Hz, 2H), 7.09 (d, J = 8.7 Hz, 2H), 7.28−7.48 (m, 6H), 7.79−7.88 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 10.6, 32.3, 55.2, 56.6, 113.7, 127.5, 128.1, 128.2, 128.3, 128.5, 131.6, 131.7, 131.8, 132.4, 132.6, 135.5, 158.4; MS (CI) 365 (M^+), 336 (M − CH_2CH_3), 201 (Ph_2PO^+), 164 (M − Ph_2PO). Anal. Calcd for $C_{22}H_{24}NO_2P$: C, 72.31; H, 6.62; N, 3.83. Found: C, 72.61; H, 6.64; N, 3.72. The (*S*)-isomer (major product) was obtained in 90% ee as determined by HPLC (Chiracel AD column, hexane/propan-2-ol = 80/20; flow rate = 1 mL/min; (*R*)-isomer, t_R = 10.35 min; (*S*)-isomer, t_R = 17.59 min).

***N*-(1-Piperonylpropyl)-*P,P*-diphenylphosphinoylamide (10e).** This compound (28.4 mg, 0.075 mmol, 75%) was obtained as a white solid: mp 149−150 °C; IR (Nujol) cm^{-1} 3227, 1192; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 0.78 (t, J = 7.4 Hz, 3H), 1.73−1.85 (m, 1H), 1.91−2.05 (m, 1H), 3.25 (m, 1H), 4.02−4.04 (m, 1H), 5.94−5.95 (m, 2H), 6.55−6.59 (m, 1H), 6.69−6.71 (m, 2H), 7.35−7.48 (m, 6H), 7.75−7.95 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 10.5, 32.4, 56.9, 100.9, 106.7, 107.9, 119.9, 128.1, 128.2, 128.3, 128.4, 131.5, 131.6, 131.7, 131.8, 132.3, 132.4, 132.5, 134.0, 137.5, 146.4, 147.6; MS (CI) 379 (M^+), 350 (M − CH_2CH_3), 216 (Ph_2PONH^+), 201 (Ph_2PO^+), 178 (M − Ph_2PO); 137.4 (Ar). Anal. Calcd for $C_{22}H_{22}NO_3P$: C, 69.65; H, 5.84; N, 3.69. Found: C, 69.79; H, 5.90; N, 3.59. The (*S*)-isomer (major product) was obtained in 90% ee as determined by HPLC (Chiracel AD column, hexane/propan-2-ol = 80/20; flow rate = 1 mL/min; (*R*)-isomer, t_R = 11.05 min; (*S*)-isomer, t_R = 17.59 min).

***N*-[1-(4′-Methylphenyl)propyl]-*P,P*-diphenylphosphinoylamide (10f).** This compound (25.0 mg, 0.072 mmol, 72%) was obtained as a white solid: mp 158−159 °C; IR (Nujol) cm^{-1} 3224, 1185; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 0.78 (t, J = 7.4 Hz, 3H), 1.78−1.90 (m, 1H), 1.95−2.09 (m, 1H), 2.35 (s, 3H), 3.30−3.33 (m, 1H), 4.05−4.14 (m, 1H), 7.06 (d, J = 8.1 Hz, 2H), 7.12 (d, J = 8.1 Hz, 2H), 7.35−7.48 (m, 6H), 7.75−7.89 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 10.5, 21.0, 32.4, 56.9, 126.3, 128.1, 128.3, 128.4, 129.1, 131.6, 131.7, 131.8, 132.4, 132.5, 132.6, 136.6, 140.4; MS (CI) 320 (M − CH_2CH_3), 201 (Ph_2PO^+), 148 (M − Ph_2PO). Anal. Calcd for $C_{22}H_{24}NOP$: C, 75.62; H, 6.92; N, 4.01. Found: C, 75.52; H, 6.89; N, 4.18. The (*S*)-isomer (major product) was obtained in 93% ee as determined by HPLC (Chiracel AD column, hexane/propan-2-ol = 92/8; flow rate = 1 mL/min; (*R*)-isomer, t_R = 21.83 min; (*S*)-isomer, t_R = 27.42 min).

***N*-[1-(3-Methylphenyl)propyl]-*P,P*-diphenylphosphinoylamide (10g).** This compound (23.8 mg, 0.068 mmol, 68%) was obtained as a white solid: mp 133−134 °C; IR (Nujol) cm^{-1} 3135, 1197; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 0.78 (t, J = 7.3 Hz, 3H), 1.79−1.91 (m, 1H), 1.95−2.06 (m, 1H), 2.32 (s, 3H), 3.30−3.33 (m, 1H), 4.02−4.09 (m, 1H), 6.92−7.07 (m, 3H), 7.20−7.27 (m, 1H), 7.35−7.48 (m, 6H), 7.77−7.88 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 10.5, 21.4, 32.3, 57.1, 123.4, 127.3, 127.7, 128.1, 128.2, 128.3, 128.4, 131.6, 131.7, 131.8, 132.5, 132.6, 137.9, 143.2, 143.3; MS (CI) 320 (M − CH_2CH_3), 258 (M − $CH_3C_6H_4$), 201 (Ph_2PO^+), 148 (M − Ph_2PO). Anal. Calcd for $C_{22}H_{24}NOP$: C, 75.62; H, 6.92; N, 4.01. Found: C, 75.89; H, 6.92; N, 3.99. The (*S*)-isomer (major product) was obtained in 93% ee as determined by HPLC (Chiracel AD column, hexane/propan-2-ol = 90: 10; flow rate = 1 mL/min; (*R*)-isomer, t_R = 10.96 min; (*S*)-isomer, t_R = 20.88 min).

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Supporting Information Available: ^{1}H NMR spectra of new compounds **4a**−**l**, **6a, 6c, 6d, 6f, 6g, 6j**, **9e, 9f**, **10e**, and **10f**. X-ray spectra of **4f** and **4j**. This material is available free of charge via the Internet at http://pubs.acs.org.

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