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Diastereomeric Resolution of *rac*-1,1′-Bi-2-naphthol Boronic Acid with a Chiral Boron Ligand and Its Application to Simultaneous Synthesis of (*R*)- and (*S*)-3,3′-Disubstituted 1,1′-Bi-2-naphthol Derivatives

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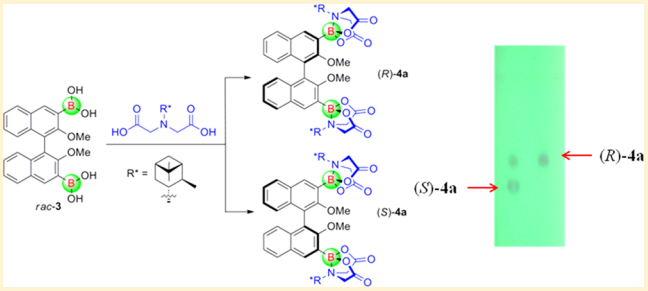
Supporting Information

ABSTRACT: A new concept of diastereomeric resolution has been developed where a boronic acid functionality was employed as (1) a diastereomeric resolving group with a chiral boron ligand and (2) a masked functional group for further transformation thereafter. This new diastereomeric resolution method was successfully applied to the preparation of both (*R*)- and (*S*)-3,3′-disubstituted 1,1′-bi-2-naphthol (BINOL) derivatives in a step-ecomonical manner. Racemic BINOL boronic acid reacted with a commercially available pinene-derived iminodiacetic acid as a chiral boron ligand to generate the two diastereomers in quantitative yields over a gram-scale quantity. After the removal of the chiral boron ligand from the diastereomers under mild conditions, the subsequent Suzuki coupling reaction of the resulting chiral BINOL boronic acids with aryl halides provided a series of both (*R*)- and (*S*)-BINOL derivatives in good yields. Further, both resulting diastereomers could be directly applied to the Suzuki coupling reaction without the removal of the chiral ligand.



INTRODUCTION

Diastereomeric resolution of racemic compounds with a chiral auxiliary has been considered one of the most commonly used methods for the preparation of enantiomerically pure compounds and thus is actually an important tool in the preparation of optically active drugs in the pharmaceutical industry.[1] In conventional diastereomeric resolutions, a functional group ($\mathbf{FG_1}$) in a racemic compound is utilized as a diastereomeric resolving group with a chiral auxiliary to afford two diastereomers. Subsequent removal of the auxiliary from the resulting diastereomers furnishes the original compound in an enantiomerically pure form, and the further derivatization of the resulting enantiomers is generally performed using other functional group than $\mathbf{FG_1}$ (Scheme 1a). In contrast, we envisioned that if a functional group ($\mathbf{FG_1}$) in a racemic compound were initially utilized as a resolving group with a chiral auxiliary and the same functional group in the resulting enantiomers and/or diastereomers could be further functionalized thereafter, enantiomerically pure compounds would be more readily derivatized (Scheme 1b). Furthermore, if this approach could be applied to the diastereomeric resolution of an advanced intermediate derived from a racemic starting material rather than that of the racemic starting material, both enantiomers of a product could be readily obtained in a step-economical manner in case both enantiomers of the product needed to be prepared. In order to demonstrate the feasibility of this new diastereomeric resolution method, we chose a diastereomeric resolution of a racemic BINOL boronic acid where a boronic acid is utilized as a dual role functional group; the boronic acid initially acts as a diastereomeric resolution group with a chiral boron ligand[2] and then is utilized to introduce substituents at the 3,3′-position of the BINOL backbone.

Since the first use of a chiral BINOL as a ligand for metal-mediated catalysis in 1979,[3] BINOL has been considered one of the commonly used privileged ligands[4] in metal-based asymmetric Lewis acid catalysis. More recently, they have been also considered as important frameworks in asymmetric organocatalysis: chiral BINOLs have been used not only as hydrogen bonding catalysts[5] but also as key chiral scaffolds in phosphoric acid catalysis.[6] Since the outcome of a given asymmetric transformation strongly depends on the electronic and steric properties of the BINOL framework, significant efforts have been made to develop BINOL derivatives by introducing substituents within the BINOL periphery.[7] Among the BINOL derivatives developed, 3,3′-disubstituted BINOL derivatives, (*R*)-**1** and (*S*)-**1** (Figure 1), have been most widely utilized in asymmetric catalysis,[8] and thus the development of efficient methods for the synthesis of enantiomerically pure 3,3′-disubstituted BINOL derivatives is of considerable importance.

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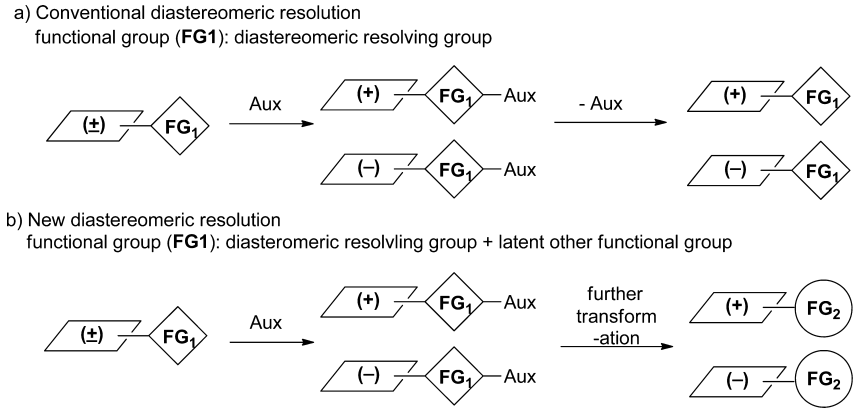
Scheme 1. Diastereomeric Resolution of Racemic Compounds



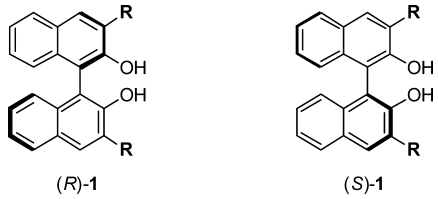
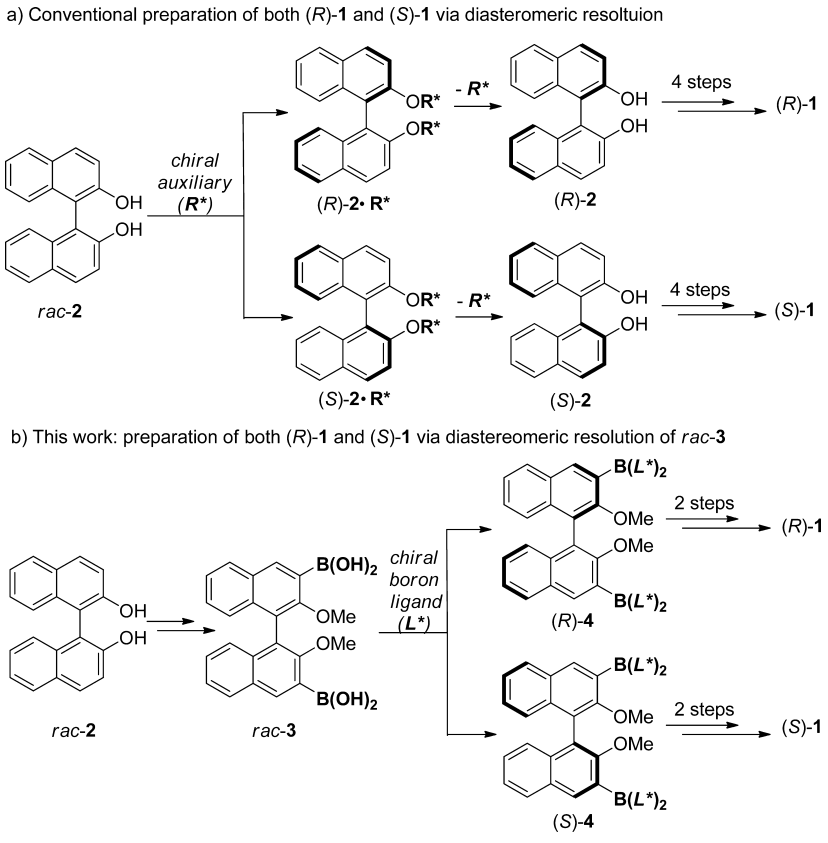


Figure 1. Structures of (*R*)- and (*S*)-3,3′-disubstituted BINOL derivatives ((*R*)-**1** and (*S*)-**1**).

In conventional methods for the synthesis of 3,3′-disubstituted chiral BINOL derivatives via diastereomeric resolution, *racemic*-BINOL, *rac*-**2**, is resolved with a chiral auxiliary using the hydroxyl functionality on the BINOL backbone. After the isolation of one enantiomer of BINOL, the subsequent introduction of substituents at the 3,3′-positions of the BINOL backbone is carried out to access optically pure 3,3′-disubstituted BINOLs (Scheme 2a). However, in order to access the other enantiomers of BINOL derivatives, the same synthetic sequence must be performed with the other enantiomer of BINOL.[9] On the other hand, *racemic*-BINOL derivative *rac*-**3**, bearing a boronic acid functionality at the 3,3′-position,[10] could undergo diastereomeric resolution with a chiral ligand on the boron.[2] After the separation of the resulting diastereomers, subsequent Suzuki reaction of the boronic acid functionality in the diastereomers and/or enantiomers would provide both (*R*)-**1** and (*S*)-**1** after deprotection of the methyl

Scheme 2. (a) Conventional Approach To Access Both (*R*)-1 and (*S*)-1 via Diastereomeric Resolution. (b) Our Approach for Both (*R*)-1 and (*S*)-1 via Diastereomeric Resolution of *rac*-3



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ether group (Scheme 2b). Furthermore, since an advanced intermediate derived from *racemic*-BINOL rather than *racemic*-BINOL itself is applied to diastereomeric resolution, both (*R*)-**1** and (*S*)-**1** can be more readily accessed in a step-economical manner as compared to the conventional diastereomeric resolution.

Herein we would like to report a novel diasteromeric resolution method using a boronic acid functionality as a diastereomeric resolving group and a latent functional group for further transformation. In addition, this diastereomeric resolution has been successfully applied to the step-economical synthesis of both (*R*)- and (*S*)-BINOL derivatives from *rac*-BINOL boronic acid. To the best of our knowledge, this is the first example of utilizing a boronic acid functionality to resolve the *racemic*-BINOL compounds rather than the hydroxy group. Furthermore, this is the first example of the preparation of chiral BINOL derivatives via diastereoselective resolution of an advanced intermediate stage from *racemic*-BINOL rather than the *racemic*-BINOL stage.

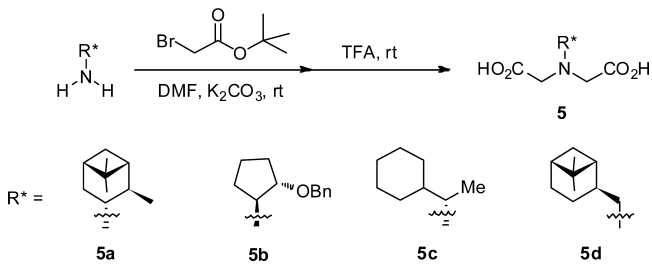
RESULTS AND DISCUSSION

The key for the success of this approach is the choice of a chiral ligand on the boron atom in the boronic acid in *rac*-**3**. The chiral ligand (1) should generate the two stable diastereomers with *rac*-**3**, displaying large difference in their physical properties, which enables us to separate them by conventional separation methods; (2) should be easily removed; and (3) should be recovered by a simple workup procedure if possible.

Considering these requirements, we commenced with our studies to find a suitable chiral ligand on the boronic acid moiety in *rac*-**3**. First, we focused on finding a suitable scaffold to provide enough stability to the resulting boronates. Recently, the Burke group has developed a trivalent *N*-methyliminodiacetate (MIDA) ligand,[11] which significanlty increases the stability of boronic acids for Suzuki coupling reactions that would have otherwise resulted in poor or negligible yields.[12−14] Furthermore, the increased stability of MIDA boronates allowed the isolation and storage of problematic heteroaromatic boronic acids.[15] On the basis of these results, we chose the MIDA motif as a basic scaffold for the chiral ligand on the boron in *rac*-**3** to provide stability of the resulting boronates. Next, we moved our attention to the design of the chiral ligands by incorportating chirality on the MIDA scaffold, which should be critical in achieving better diastereomeric resolution. X-ray structures of MIDA boronates showed that the methyl group in the MIDA ligand is closely positioned to the π-aryl substrates.[12] Thus, we expected that chiral ligands incorporating chirality on the *N*-alkyl group in the MIDA scaffold might lead to better diastereomeric resolution of *rac*-**3** due to the proximity betwen the chiral motif and the axially chiral center in the BINOL backbone. Furthermore, very recently the Burke group has developed new chiral boron ligands bearing chirality in the *N*-alkyl moiety and applied the chiral MIDA ligands to the diastereoselective epoxidation of alkenyl boronates.[16] On the basis of these considerations, we decided to first explore the diastereomeric resolution of *rac*-**3** using chiral boron ligands **5a−d** developed by the Burke group. Chiral boron ligands **5a−d** could be readily prepared by following the literature procedure with slight modifications on a multigram scale from commodity chemicals, such as chiral amines, *tert*-butyl bromoacetate, and trifluoroacetic acid (Scheme 3).[16]

With these chiral boron ligands **5a−d** in hand, the diastereomeric resolution of *rac*-**3** with these ligands was

Scheme 3. Preparation of Chiral Boron Ligands 5a−d Bearing Chirality on the *N*-Alkyl Moiety



investigated (Table 1). The chiral scaffold in the ligands was found to have a significant effect on the resolution of the resulting diastereomers. The chiral ligands **5a** and **5b**, derived from pinene and cyclopentyl amines, respectively, afforded the two diastereomers in high yields after column chromatography (entries 1 and 2), while the diastereomers with other chiral ligands **5c** and **5d** were obtained as inseparable mixtures (entries 3 and 4).[17] Although both chiral ligand **5a** or **5b** were effective in the diastereomeric resolution of *rac*-**3**, we decided to use pinene-derived iminodiacetic acid ligand **5a** as the chiral boron ligand because of its commercial availability.[18]

To test the practicality of this method, we carried out the diastereomeric resolution of *rac*-**3** with **5a** on a gram scale (Scheme 4). To our satisfaction, both diastereomers (*R*)-**4a** and (*S*)-**4a** were obtained in high yields without any loss of efficiency (eq 1). Furthermore, **5a** was easily removed from (*R*)-**4a** under mild aqueous basic solution and quantitatively recovered by simple aqueous extraction (eq 2). Moreover, the recovered **5a** could be directly reapplied to diastereomeric resolution of *rac*-**3** without any loss of efficiency.

After successful diastereomeric resolution, we attempted to introduce substitutents at the 3,3′-position through direct application of the resulting (*R*)- and (*S*)-enantiomers of the BINOL boronic acid to Suzuki coupling reaction with aryl bromides **6** (Table 2),[19] which could be one of the advantages of our new diasteromeric resolution method as compared to the previously developed methods. Delightedly, both BINOL derivatives, (*R*)-**1a** and (*S*)-**1a**, bearing a 4-biphenyl group were obtained in good yields (entries 1 and 2). Under these conditions, various aromatic bromides were successfully applied to Suzuki reaction with (*R*)-**3**. Electronic properties had little effect on the reaction yields; both electron-rich and electron-deficient aryl halides provided the desired Suzuki coupling products in good yields (entries 1, 3−7). However, steric bulkiness produced a detrimental effect on the cross-coupling reaction: 2,6-disubstituted aryl bromides, such as mesityl bromide, provided the desired product in only moderate yield along with the monocoupled as well as deboronated products (entry 8).[20] In order to demonstrate the effectiveness of this method, we needed to varify that the BINOL derivatives obtained by this method are be enantiomerically pure, and that there is no racemization during the hydrolysis of chiral boron ligand **5a** and/or cross-coupling reaction of the resulting boronic acids. Thus, we decided to determine the enantiopurity of the resulting BINOL derivatives. Initially, we attempted to determine the enantiopurity of of compounds (*R*)-**1a** and (*S*)-**1a** but were not able to separate the two enantiomers using our chiral HPLC system. When the hydroxy groups in (*R*)-**1a** and (*S*)-**1a** were protected as a methyl group, both compounds were obtained as a single enantiomer, and the other enantiomer

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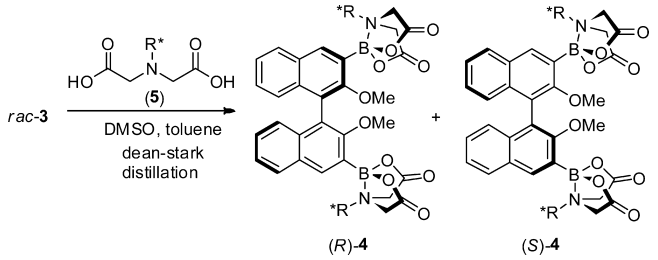
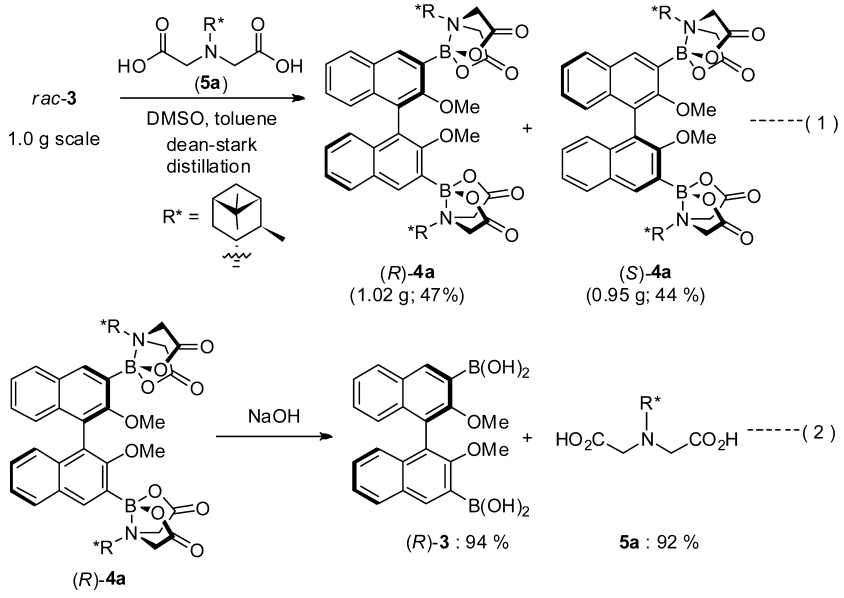
Table 1. Diastereomeric Resolution of *rac*-3 with Chiral Boron Ligands 5a–d[a]



entry	5	eluent	product[b]	R_f	yield (%)	$[\alpha]_D$
1	**5a**	Hx/EtOAc (1:2)	(*R*)-**4a**	0.4	45	−230.7 (−158.5)[c]
			(*S*)-**4a**	0.3	41	234.8 (159.4)[c]
2	**5b**	Hx/EtOAc (1:3)	(*R*)-**4b**	0.6	47	−90.0 (−157.9)[c]
			(*S*)-**4b**	0.3	45	88.5 (158.8)[c]
3	**5c**	Hx/EtOAc (1:1)	(*R*)-**4c**	0.3	ND[d]	ND[d]
			(*S*)-**4c**	0.3	ND[d]	ND[d]
4	**5d**	Hx/EtOAc (1:2)	(*R*)-**4d**	0.3	ND[d]	ND[d]
			(*S*)-**4d**	0.3	ND[d]	ND[d]

[a]Conditions: *rac*-**3** (0.25 mmol), ligand **5** (0.75 mmol), DMSO/toluene (1:10), reflux, 12 h. [b]The absolute configuration was determined by comparison of R_f value and optical rotation of (*R*)-**4** derived from optically pure (*R*)-**3**. [c]The values in parentheses are optical rotation of (*R*)-**3** and (*S*)-**3** after removal of chiral ligand **5**. [d]Not determined.

Scheme 4. Diastereomeric Resolution of *rac*-3a with 5a on a Gram Scale and Removal of 5a



was not observed in the HPLC analysis. Thus, we confirmed that there was no racemization during hydrolysis of chiral boron ligand **5a** and/or cross-coupling reaction of the resulting boronic acids.[17]

Next, we attempted to directly apply the diastereomer (*R*)-**4a** to the Suzuki reaction with 4-biphenyl bromide **6a** without removal of the chiral ligand (Scheme 5). On the basis of the conditions developed by the Burke group,[13] we investigated several reaction parameters. Interestingly, the choice of phosphine ligand had a strong influence on the reaction yield. Among the phosphine ligands tested, XPhos provided the best result,[21] and the desired product (*R*)-**1a** was obtained in comparable yield with that from (*R*)-**3** even without further optimization of reaction conditions (eq 3). Furthermore, the Suzuki coupling reaction of the other diastereomer (*S*)-**4a** with **6a** also provided (*S*)-**1a** in yield similar to that obtained with the reaction with (*R*)-**4a** (eq 3′).

In conclusion, we have demonstrated a new diastereomeric resolution where a functional group in a racemic compound played a dual-role: (1) the diastereomeric resolution with a chiral auxiliary and (2) further transformation in the resulting diastereomers and/or enantiomers. The usefulness of new diastereomeric resolution method was successfully demonstrated to the synthesis of both (*R*)- and (*S*)-3,3′-disubstituted BINOL derivatives via the diastereomeric resolution of *rac*-**3** with a commercially available pinene-derived iminodiacetic acid ligand **5a**, followed by a Suzuki coupling reaction. Various aryl groups could be easily introduced via subsequent Suzuki coupling reaction in good yields. Moreover, both (*R*)- and (*S*)-diastereomers, (*R*)-**4a** and (*S*)-**4a**, could be directly applied to the Suzuki coupling reaction without the removal of the chiral

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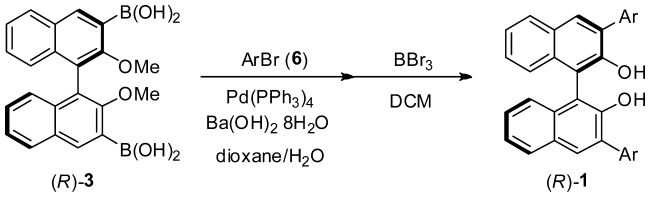
Table 2. Preparation of Chiral 3,3′-Disubstituted BINOL via Suzuki Coupling Reaction[a]

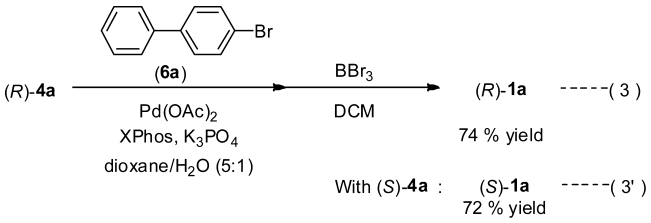


(*R*)-**3** (*R*)-**1**

entry	ArBr (**6**)	product	yield (%)[b]
1	4-PhC_6H_4	(*R*)-**1a**	79
2[c]	4-PhC_6H_4	(*S*)-**1a**	77
3	C_6H_5	(*R*)-**1b**	71
4	3,5-$(CH_3)_2C_6H_3$	(*R*)-**1c**	76
5	4-$(NO_2)C_6H_4$	(*R*)-**1d**	78
6	3,5-$(CF_3)_2C_6H_3$	(*R*)-**1e**	79
7	2-naphthyl	(*R*)-**1f**	70
8	2,4,6-$(CH_3)_3C_6H_2$	(*R*)-**1g**	28

[a]Conditions: (*R*)-**3** (0.20 mmol), aryl bromide **6** (0.64 mmol), $Pd(PPh_3)_4$ (0.01 mmol), $Ba(OH)_2{\cdot}8H_2O$ (0.58 mmol) in dioxane/H_2O (5:1) was refluxed for 12 h. [b]Determined after deprotection of the OMe group. [c](*S*)-**3** was used instead.

Scheme 5. Direct Suzuki Reaction of (*R*)-4a with 6a without Removal of 5a



ligand. It is noted that the diastereomeric resolution of an advanced intermediate such as *rac*-**3** and direct application of the boronic acid functionality to the Suzuki reaction allowed us to access both (*R*)- and (*S*)-BINOL derivatives in a step-economical manner. Moreover, ready availability of all the starting compounds (*rac*-**3** and **5a**) and a simple procedure would render this method highly attractive to the synthetic community. Further application of this new diastereomeric resolution methed to asymmetric synthesis is underway in our research group.

EXPERIMENTAL SECTION

General. All reactions were carried out in oven- or flame-dried glassware under nitrogen atmosphere unless otherwise noted. Except as otherwise indicated, all reactions were magnetically stirred and monitored by analytical thin layer chromatography (TLC) using precoated silica gel glass plates (0.25 mm) with F254 indicator. Visualization was accomplished by UV light (254 nm), with combination of potassium permanganate and/or phosphomolybdic acid solution as an indicator. Flash column chromatography was performed according to the method of Still using silica gel 60 (230–400 mesh). Yields refer to chromatographically and spectrographically pure compounds, unless otherwise noted. Commercial grade reagents and solvents were used without further purification. *rac*-(2,2′-Dimethoxy-[1,1′-binaphthalene]-3,3′-diyl)diboronic acid (*rac*-**3**) was synthesized by following literature procedure.[10] ^{1}H NMR and ^{13}C NMR spectra were recorded on 300 and 100 MHz NMR spectrometers, respectively. Tetramethylsilane and the solvent resonance were used as internal standards for ^{1}H NMR (δ 0.0 ppm) and ^{13}C NMR, respectively. The proton spectra are reported as follows δ (position of proton, multiplicity, coupling constant *J*, number of protons). Multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (quintet), h (septet), m (multiplet), and br (broad). High resolution mass spectra (HRMS) were obtained using quadrupole instrucment with FAB as the ionization method. The optical rotations were measured on an automatic polarimeter. Enantiomeric excesses were determined by HPLC analysis using a chiral column (Chiralpak OD-H, ϕ 4.6 mm × 250 mm) with a mixture of hexanes and isopropyl alcohol as an eluent.

General Procedure for Synthesis of Chiral Boron Ligands 5. To a stirred solution of a chiral amine (32.6 mmol; 1.00 equiv.), K_2CO_3 (13.5 g, 97.9 mmol; 3.00 equiv.) in DMF (50 mL) was added *tert*-butyl-2-bromoacetate (19.1 g, 97.9 mmol; 3.00 equiv) at room temperature. The reaction mixture was stirred at room temperatur and monitored by TLC. After 24 h, the reaction was quenched with water and extracted with EtOAc (3 × 100 mL). The combined organic layer was dried with $MgSO_4$ and concentrated under reduced pressure. The residue was dissolved in dichloromethane (100 mL), and then trifluoroacetic acid (25 mL, 326 mmol, 10.0 equiv) was added to the solution dropwise at 0 °C. After 48 h, reaction mixture was concentrated *in vacuo* and recrystallized in Et_2O to afford the desired product **5**.

*2,2′-(((1R,2R,3R,5S)-2,6,6-Trimethylbicyclo[3.1.1]heptan-3-yl)-azanediyl)diacetic Acid (**5a**).*[16] Yield: 5.24 g (60.0%). White solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.63 (s, 4H), 3.40–3.38 (m, 1H), 2.30–2.22 (m, 2H), 1.90–1.67 (m, 4H), 1.16 (s, 3H), 1.07 (d, *J* = 6.6 Hz, 3H), 0.93 (s, 3H), 0.86 (d, *J* = 9.9 Hz, 1H).

*2,2′-(((1S,2S)-2-(Benzyloxy)cyclopentyl)azanediyl)diacetic Acid (**5b**).*[16] Yield: 4.43 g (44.2%). White solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.42–7.23 (m, 5H), 4.45–4.34 (m, 2H), 3.79–3.40 (m, 1H), 3.45 (s, 4H), 3.23–3.20 (m, 1H), 1.84–1.78 (m, 2H), 1.65–1.39 (m, 3H), 1.38–1.26 (m, 1H).

*(S)-2,2′-((1-Cyclohexylethyl)azanediyl)diacetic Acid (**5c**).*[16] Yield: 3.97 g (50.1%). White solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.45–3.31 (m, 4H), 2.44–2.38 (m, 1H), 1.93 (app d, *J* = 12.9 Hz, 1 H), 1.65–1.58 (m, 4H), 1.27–1.09 (m. 5H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.86–0.78 (m, 1H).

*2,2′-((((1R,2S,5R)-6,6-Dimethylbicyclo[3.1.1]heptan-2-yl)methyl)-azanediyl)diacetic Acid (**5d**).*[16] Yield: 5.29 g (60.3%). White solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.42 (s, 4H), 2.63 (d, *J* = 6.6 Hz, 2H), 2.32–2.19 (m, 1H), 2.18–2.09 (m, 1H), 1.99–1.75 (m, 5H), 1.59–1.47 (m, 1H), 1.14 (s, 3H), 0.92 (s, 3H), 0.86 (d, *J* = 9.1 Hz, 1H).

General Procedures for Diastereomeric Resolution of *rac*-3 with Chiral Boron Ligand 5 (Table 1). To a solution of *rac*-**3** (0.10 g; 0.25 mmol; 1.0 equiv) in a mixture of DMSO and toluene (1:10, 3 mL) was added a chiral ligand **5** (0.75 mmol; 3.0 equiv). The reaction mixture was refluxed with azeotropic removal of water using Dean–Stark condenser under air atmosphere. After 12 h, the reaction mixture was cooled to room temperature. The reaction mixture was quenched with water and extracted with EtOAc. The organic layer was combined, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography on silica eluting with EtOAc/hexane to give the corresponding (*R*)-**4** and (*S*)-**4**.

(*R*)-**4a**. Yield: 97 mg (45%); 1.0 g (47%) in 2.5 mmol scale reaction. R_f = 0.4 (EtOAc/hexanes = 2:1). A white solid. ^{1}H NMR (300 MHz, DMSO-d$_6$) δ 8.36 (s, 2H), 8.07 (d, *J* = 8.2 Hz, 2H), 7.43 (t, *J* = 7.1 Hz, 2H), 7.20 (t, *J* = 7.1 Hz, 2H), 7.13 (d, *J* = 8.3 Hz, 2H), 4.56–4.06 (m, 8H), 3.70–3.59 (m, 2H), 3.12 (s, 6H), 2.42–2.25 (m, 4H), 1.78–1.60 (m, 6H), 1.54–1.49 (m, 2H), 1.19 (d, *J* = 6.6 Hz, 6 H), 1.09 (s, 6 H), 1.00–0.97 (m, 2H), 0.76 (s, 6H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.9, 168.4, 159.8, 137.9, 136.0, 130.5, 129.5, 128.1, 125.6, 125.5, 123.5, 68.9, 62.2, 61.2, 56.6, 49.1, 39.0, 38.0, 31.5, 30.8, 27.2, 24.8, 23.9. $[\alpha]^{20}_D$ = −230.7 (*c* 0.25, THF). HRMS (FAB+) calcd for $C_{50}H_{58}B_2N_2O_{10}$ (M^+) 868.4278, found 868.4281.

(*S*)-**4a**. Yield: 89 mg (41%); 0.95 g (44%) in 2.5 mmol scale reaction. R_f = 0.3 (EtOAc/hexanes = 2:1). A white solid. ^{1}H NMR (300 MHz, DMSO-d$_6$) δ 8.35 (s, 2H), 8.04 (d, *J* = 8.2 Hz, 2H), 7.41 (t, *J* = 7.4 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 2H), 6.92 (d, *J* = 8.5 Hz, 2H), 4.57–3.91 (m, 8H), 3.71–3.58 (m, 2H), 2.88 (s, 6H), 2.42–2.34 (m, 2H), 2.27 (m, 2H) 1.80–1.70 (m, 6H), 1.56–1.52 (m, 2H), 1.16 (d, *J*

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= 6.8 Hz, 6 H), 1.07 (s, 6 H), 0.98 (d, J = 10.7 H), 0.59 (s, 6H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 171.0, 168.7, 158.0, 137.9, 134.3, 130.5, 129.6, 127.3, 125.7, 125.2, 121.2, 68.5, 62.3, 59.6, 56.9, 49.3, 38.1, 31.4, 30.8, 27.3, 24.2, 23.6. $[\alpha]^{20}_D$ = 234.8 (c 0.25, THF). HRMS (FAB+) calcd for $C_{50}H_{58}B_2N_2O_{10}$ (M^+) 868.4278, found 868.4271.

(*R*)-**4b**. Yield: 110 mg (47%). R_f = 0.6 (EtOAc/hexanes = 3:1). A white solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.27 (s, 2H), 8.04 (d, J = 8.7 Hz, 2H), 7.45−7.20 (m, 14H), 7.10 (br, 2H), 4.49−4.20 (m, 14 H), 4.06 (br, 2H), 2.79 (s, 6H), 1.60−1.31 (m, 2H), 1.24−0.95 (m, 10H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 171.0, 169.3, 160.5, 138.6, 137.0, 135.3, 130.7, 130.3, 129.6, 129.1, 128.6, 128.0, 125.5, 123.9, 80.5, 73.8, 72.2, 61.8, 61.0, 30.2, 25.8, 20.3. $[\alpha]^{20}_D$ = −90.0 (c 0.25, THF). HRMS (FAB+) calcd for $C_{54}H_{54}B_2N_2O_{12}$ (M^+) 944.3863, found 944.3837.

(*S*)-**4b**. Yield: 110 mg (45%). R_f = 0.3 (EtOAc/hexanes = 3:1). A white solid, ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.30 (s, 2H), 7.99 (d, J = 8.3 Hz, 2H), 7.35−6.97 (m, 16H), 4.49−4.11 (m, 14 H), 3.49 (br, 2H), 3.06 (s, 6H), 1.96 (br, 2H), 1.53 (br, 4H), 1.28 (br, 6H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.8, 169.5, 158.1, 138.8, 137.2, 134.1, 132.3, 130.7, 129.4, 129.0, 128.3, 127.6, 125.5, 125.2, 122.5, 80.8, 74.4, 71.4, 62.0, 59.8, 57.2, 30.5, 26.7, 21.9. $[\alpha]^{20}_D$ = 88.5 (c 0.25, THF). HRMS (FAB+) calcd for $C_{54}H_{54}B_2N_2O_{12}$ (M^+) 944.3863, found 944.3871.

General Procedure for Removal and Recovery of Ligand 5a. To a solution of (*R*)-**4a** (1.02 g; 1.17 mmol) in THF (20 mL) was added 1 N NaOH (14 mL) in one portion. The reaction mixture was further stirred for 1 h at room temperature and monitored by TLC. After completion of the reaction, the reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with EtOAc. The combined organic layer was concentrated and reprecipitated in Et_2O to provide **5a** in 92% yield. Remained Et_2O layer was concentrated to provide (*R*)-**3** in 94% yield. The spectroscopic data of (*R*)-**3** were in good agreement with the literature.[10] ^{1}H NMR (300 MHz, acetone-d_6) δ 8.56 (s, 2H), 8.04 (d, J = 7.97 Hz, 2H), 7.46 (t, J = 7.42 Hz, 2H), 7.34 (t, J = 7.55 Hz, 2H), 7.11 (d, J = 8.24 Hz, 2H), 3.42 (s, 6H); $[\alpha]^{20}_D$ = −158.5 (c 0.10, $CHCl_3$), {lit.[3] $[\alpha]^{20}_D$ = −153.4 (c 1, $CHCl_3$)}.

General Procedure for Suzuki Cross-Coupling Reaction of (*R*)-3 with Aryl Bromides 6 (Table 2). In a 20-mL pressure vessel equipped with a magnetic stirring bar were added (*R*)-**3** (80 mg, 0.20 mmol, 10 equiv), $Ba(OH)_2{\cdot}8H_2O$ (180 mg, 0.58 mmol, 2.9 equiv), $Pd(PPh_3)_4$ (12 mg, 0.010 mmol, 0.050 equiv), and the relevant aryl bromide (0.64 mmol, 3.2 equiv) in 1,4-dioxane (5.0 mL) and H_2O (2.0 mL), and the vessel was filled with N_2. The reaction mixture was stirred for 24 h at 120 °C and cooled to room temperature. Then 1 N HCl (30 mL) was added and extracted with dichloromethane (3 × 50 mL). The organic layer was combined, dried over $MgSO_4$, and concentrated *in vacuo* to give a crude oil. To the crude product solution in anhydrous dichloromethane (10 mL) was added a solution of BBr_3 (0.11 mL, 1.1 mmol, 5.5 equiv) in dichloromethane dropwise at 0 °C. The reaction mixture was warmed to room temperature and stirred for an additional 20 h. After completion of the reaction, the reaction mixture was quenched with water at 0 °C and extracted with dichloromethane. The organic layer was combined, washed with brine (30 mL) and water (30 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography over silica gel to give (*R*)-**1**.

*(R)-3,3′-Bis(4-biphenyl)-2,2′-dihydroxy-1,1′-dinaphthyl ((R)-**1a**).*[19] Yield: 93 mg (79%). R_f = 0.3 (dichloromethane/hexanes = 1:3). A white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (s, 2H), 7.95 (d, J = 7.97 Hz, 2H), 7.86−7.83 (m, 4H), 7.73 (d, J = 8.24 Hz, 4H), 7.67 (d, J = 7.69 Hz, 4H), 7.50−7.31 (m, 12H), 5.44 (s, 2H). $[\alpha]^{20}_D$ = −50.4 (c 0.400, $CHCl_3$), {lit.[19] $[\alpha]^{20}_D$ = −70.3 (c 1, $CHCl_3$)}.

*(S)-3,3′-Bis(4-biphenyl)-2,2′-dihydroxy-1,1′-dinaphthyl ((S)-**1a**).*[9a] (*S*)-**3** was used instead of (*S*)-**3**. Yield: 91 mg (77%). R_f = 0.3 (dichloromethane/hexanes = 1:3). A white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (s, 2H), 7.95 (d, J = 7.97 Hz, 2H), 7.86−7.83 (m, 4H), 7.73 (d, J = 8.24 Hz, 4H), 7.67 (d, J = 7.69 Hz, 4H), 7.50−7.31 (m, 12H), 5.42 (s, 2H); $[\alpha]^{20}_D$ = 45.06 (c 0.400, $CHCl_3$), {lit.[9a] $[\alpha]^{20}_D$ = 55.1 (c 1.0, $CHCl_3$)}.

*(R)-3,3′-Diphenyl-2,2′-dihydroxy-1,1′-dinaphthyl ((R)-**1b**).*[19] Yield: 62 mg (71%). R_f = 0.3 (dichloromethane/hexanes = 1:1). A white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (s, 2H), 7.93 (d, J = 7.97 Hz, 2H), 7.74 (d, J = 7.14 Hz, 4H), 7.52−7.22 (m, 12H), 5.36 (s, 2H).

*(R)-3,3′-Bis(3,5-dimethylphenyl)-2,2′-dihydroxy-1,1′-dinaphthyl ((R)-**1c**).*[19] Yield: 75 mg (76%). R_f = 0.3 (dichloromethane/hexanes = 1:1). A white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (s, 2H), 7.91 (d, J = 8.00 Hz, 2H), 7.40−7.21 (m, 10H), 7.06 (s, 2H), 5.39 (s, 2H).

*(R)-3,3′-Bis(4-nitrophenyl)-2,2′-dihydroxy-1,1′-dinaphthyl ((R)-**1d**).*[22] Yield: 78 mg (74%). R_f = 0.2 (dichloromethane/hexanes = 1:1). A white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.34 (d, J = 8.24 Hz, 4H), 8.11 (s, 2H), 8.03−7.92 (m, 6H), 7.50−7.37 (m, 4H), 7.22(d, J = 8.24 Hz, 2H), 5.37 (s, 2H).

*(R)-3,3′-Bis(3,5-bis(trifluoromethyl)phenyl)-2,2′-dihydroxy-1,1′-dinaphthyl ((R)-**1e**).*[23] Yield: 110 mg (79%). R_f = 0.2 (dichloromethane/hexanes = 1:1). A white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.23 (s, 4H), 8.12 (s, 2H), 8.00 (d, J = 7.69 Hz, 2H), 7.91 (s, 2H), 7.51−7.40 (m, 4H), 7.25−7.22(m, 2H), 5.38 (s, 2H).

*(R)-3,3′-Di(2-naphthyl)-2,2′-dihydroxy-1,1′-dinaphthyl ((R)-**1f**).*[19] Yield: 76 mg (70%). R_f = 0.3 (dichloromethane/hexanes = 1:1). A white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.22 (s, 2H), 8.15 (s, 2H), 8.00−7.87 (m, 8H), 7.54−7.31 (m, 12H), 5.48 (s, 2H).

*(R)-3,3′-Bis(2,4,6-trimethyl)-2,2′-dihydroxy-1,1′-dinaphthyl ((R)-**1g**).*[22] Yield: 29 mg (28%). R_f = 0.3 (dichloromethane/hexanes = 1:1). A white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, J = 7.69 Hz, 2H), 7.74 (s, 2H), 7.41−7.29 (m, 6H), 7.01 (s, 4H), 5.00 (s, 2H), 2.34 (s, 6H), 2.14 (s, 6H), 2.07 (s, 6H).

General Procedures for Suzuki Coupling Reaction of (*R*)-4a with 4-Bromobiphenyl 6a without Removal of Ligand 5a. In a 10-mL pressure vessel were placed (*R*)-**4a** (47 mg, 0.050 mmol, 1.0 equiv), K_3PO_4 (0.16 g, 0.75 mmol, 15 equiv), $Pd(OAc)_2$ (1.2 mg, 0.0050 mmol, 0.10 equiv), biphenyl bromide **6a**, (23.3 mg, 0.10 mmol, 2.0 equiv), and X-Phos (0.010 mmol, 0.20 equiv) in 1,4-dioxane (1.0 mL) and H_2O (0.20 mL), and the vessel was filled with N_2. The reaction mixture was stirred for 24 h at 120 °C and cooled to room temperature. The reaction mixture was quenched with 1 N HCl (5 mL) and extracted with dichloromethane (3 × 10 mL). The organic layer was combined, dried over $MgSO_4$, and concentrated *in vacuo* to give crude oil. To the crude product solution in anhydrous dichloromethane (2 mL) was added BBr_3 (0.28 mL, 0.28 mmol, 5.5 equiv) dropwise at 0 °C. The reaction mixture was warmed to room temperature and stirred for an additional 20 h. After the completion of the reaction, the reaction mixture was quenched with water at 0 °C and extracted with dichloromethane. The organic layer was combined, washed with brine (10 mL) and water (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography on silica (dichloromethane/hexane 1:3) to afford (*R*)-**1a** as a white solid (yield: 22 mg (74%)). When (*S*)-**4a** was applied to the above procedure, (*S*)-**1a** was obtained as a white solid (yield: 21 mg (72%)).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Spectroscopic data for chiral boron ligands **5**, diastereomers **4**, and chiral BINOL derivatives **1**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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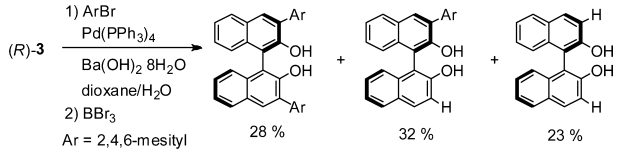

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