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Catalyzed asymmetric aryl transfer reactions to aldehydes with boroxines as aryl source

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Abstract—Asymmetric aryl transfer of triphenylboroxin to a set of aryl aldehydes has been carried out in the presence of chiral amino alcohols derived from (*S*)-proline with high enantioselectivity. Substituted phenyl boroxins were also used as aryl source in asymmetric arylation of benzaldehyde.

1. Introduction

Chiral diaryl methanols are important intermediates for the synthesis of biologically active compounds.[1] This kind of alcohol can be obtained by the catalytic asymmetric addition of aryl zinc species to aromatic aldehydes.[2] However, when compared to the tremendous progress achieved in the asymmetric addition of dialkyl zinc to aldehydes,[3] the asymmetric arylation of aldehydes using organozinc reagents is relatively unexplored because of the competitive background reaction of aryl zinc species with aromatic aldehydes directly without going through the catalytic process.[4–16]

In 1991, Soai et al. initially reported the enantioselective phenylation of prochiral aldehydes employing a zinc reagent prepared in situ from $ZnCl_2$ and phenyl magnesium bromide and stoichiometric amounts of *N*,*N*-dibutylnorephedrine.[4] Fu et al. reported, in 1997, the addition of salt-free Ph_2Zn to *p*-chlorobenzaldehyde using a planar-chiral azoferrocene ligand with moderate enantioselectivity.[5] Since then, many efforts have been dedicated to develop an efficient system for this aryl group transfer reaction. Pu et al. reported that performing the addition reaction at a low concentration of substrate improved the enantioselectivity dramatically, using chiral 3,3′-diaryl binaphthol as a ligand.[6] Bolm et al. found later that the undesired background reaction could be effectively suppressed by the concomitant use of Et_2Zn with Ph_2Zn, using ferrocyl oxazoline and rhenium-tricarbonyloxazoline as ligands.[7] In 2002, Ha et al. reported that binaphthyl based axially chiral amino alcohols showed high levels of selectivity in the addition of Ph_2Zn to aldehydes without adding Et_2Zn as an additive.[8] However, Pericas et al. found that the use of Et_2Zn/Ph_2Zn gave better results than only using Ph_2Zn in the presence of a chiral amino alcohol.[9] Very recently, Kim and Bolm reported the use of proline derived amino alcohol containing perfluoro groups for recycling purposes in the phenylation of aromatic aldehydes.[10]

In 2002, Bolm et al. broadened the scope of the aryl zinc species using aryl boronic acids as the aryl source by mixing the boronic acids with Et_2Zn or Me_2Zn at 60 °C for 10 h.[11] Recently, Braga et al. and Chan et al. also reported efficient chiral ligands for phenylation of aromatic aldehydes using phenyl boronic acid as the aryl source.[12,13] Besides aryl boronic acid, Ph_3B and alkenylborane, etc., were also used in this reaction.[14]

A threefold excess of Et_2Zn is unavoidable in the procedure of boron–zinc exchanging, since the aryl boronic acid has two additional hydroxyl groups. We assumed that Et_2Zn could tolerate the B–O bond in boroxin.[15] If so, the amount of Et_2Zn used can be reduced substantially by replacing the boronic acid by boroxin. Herein, we report an aryl transfer reaction to aromatic

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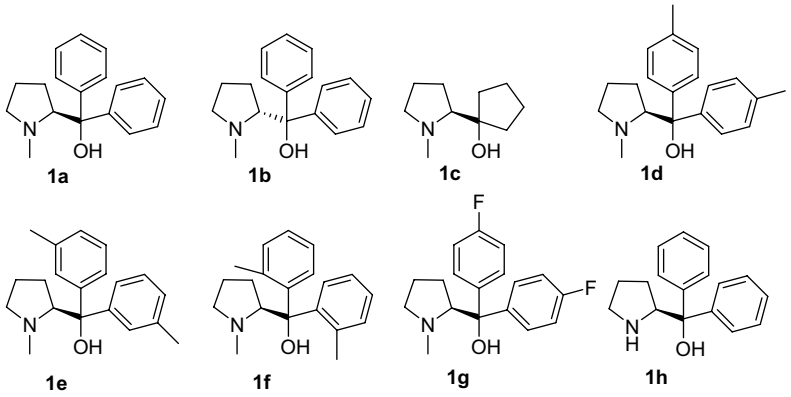


Figure 1. Amino alcohols derived from (*S*)-proline.

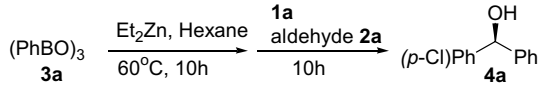
aldehydes, using aryl boroxin as the aryl source in the presence of (*S*)-proline derived amino alcohol (Fig. 1).[16]

2. Results and discussion

Systematic studies of a model reaction comprising *p*-chlorobenzaldehyde **2a**, phenyl boroxin **3a**, Et_2Zn, and ligand **1a**, are summarized in Table 1. As shown in Table 1, (*S*)-*p*-chlorobenzhydrol **4a** was formed with good enantioselectivity and high yield in the presence of **1a**. The (*S*)-configuration of the product indicates that the phenyl addition occurs at the *si*-face of the aldehyde, the same as the Et_2Zn addition catalyzed by **1a**.[17] This result suggests that the catalytic phenyl transfer reaction should be mechanistically similar to the Et_2Zn addition. Racemic **4a** was isolated in 86% yield in the absence of ligand **1a**. This result showed a strong background reaction (Table 1, entry 9). Decreasing the amount of phenyl boroxin from 0.8 to 0.4 equiv had a slightly positive effect on selectivity (90% ee), but a negative effect on the isolated yield (Table 1, entries 1 and 2). When the reaction was conducted at 10 °C, the selectivity slightly decreased from 89% ee (Table 1, entry 3) to 85% ee (Table 1, entry 4). By lowering the temperature to −15 °C, the selectivity increased slightly, 90% ee (Table 1, entry 5). The enantioselectivity dropped dramatically when the amount of **1a** was decreased to 0.02 and 0.01 equiv with 25% ee and 21% ee, respectively, due to the competitive background reaction. Although an excess of Et_2Zn was present in the reaction mixture, no ethylated product could be detected under the present reaction conditions.

Next, we examined the substituent effect of the alcohol moiety in **1a**–**h** on the level of the asymmetric induction in the addition of the phenyl zinc species to *p*-chlorobenzaldehyde **2a** (Table 2). Compound **1a** afforded the best result for this reaction. The enantiomer **1b** afforded the alcohol in 89% ee with an (*R*)-configuration. Replacing the phenyl groups in **1a** by a five-member ring caused the selectivity to decrease from 89% ee to 33% ee (Table 2, entries 1–3). The same results were reported for ethyl addition to aldehydes with the methyl group on N atom in the pyrrole ring of **1a** being vital for reactivity and selectivity.[18] Compound **1h**, a secondary amine only afforded **4a** in 84% yield and 35% ee (Table 2, entry 8). The variation of the phenyl group in **1a** can also affect the selectivity of the reaction. Compounds **1d**, **1e**, and **1f** with a methyl group on the *para*-, *meta*-, and *ortho*-position of phenyl group, respectively, catalyzed the

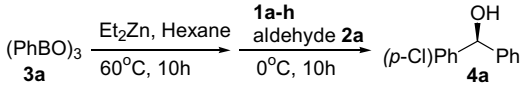
Table 1. Enantioselective phenyl transfer from phenyl boroxin to *p*-chlorobenzaldehyde **2a**[a]



Entry	Ligand **1a** (equiv)	$(PhBO)_3$ (equiv)/Et_2Zn (equiv)	Temperature (°C)	Yield (%)[b]	ee (%)[c]
1	0.1	0.8/7.2	0	95	89
2	0.1	0.4/3.6	0	88	90
3	0.1	0.66/4.0	0	91	89
4	0.1	0.66/4.0	10	90	85
5	0.1	0.67/4.0	−15	99	90
6	0.05	0.43/2.6	0	87	80
7	0.02	0.43/2.6	0	85	25
8	0.01	0.43/2.6	0	74	21
9[d]	—	0.66/4.0	0	86	—

[a] The concentration of **2a** was approximately 0.1 M.
[b] Isolated yield.
[c] Determined by chiral HPLC Chiralcel AD column.
[d] Without the addition of **1a**.

Table 2. Screening of amino alcohols **1a**–**h**[a]



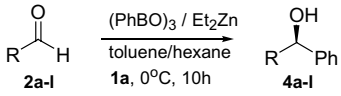
Entry	Amino alcohol	Yield (%)[b]	ee (%)[c]
1	**1a**	91	89
2	**1b**	94	89[d]
3	**1c**	91	33
4	**1d**	89	84
5	**1e**	76	85
6	**1f**	79	81
7	**1g**	85	86
8	**1h**	84	35

[a] **2a**/$(PhBO)_3$/Et_2Zn/**1a**–**h** = 1:0.66:4:0.1.
[b] Isolated yield.
[c] Determined by HPLC chiral-AD column.
[d] (*R*)-Configuration.

reaction in a slightly lower enantioselectivity than that of **1a** (Table 2, entries 4–6). Compound **1f**, containing an electron withdrawing fluoro on the *para*-position of the phenyl group gave the product alcohol in 86% ee. These results indicate that the substituent on the phenyl group of amino alcohols has little effect on the enantioselectivity.

A series of substituted benzaldehydes together with cinnamaldehyde and 1-naphthyl aldehyde were subjected to phenylation using **1a** as a ligand (Table 3). The in situ catalyst formed from **1a** and the organozinc species promoted the reaction in high yield and good enantiomeric excess for all aromatic aldehydes. *para*-Substituted benzaldehydes afford better results than that of the *meta*- and *ortho*-substituted aldehydes (Table 3, entries 1 and 3–6). According to the results reported by Bolm et al. and Chan et al., the use of DiMPEG as an additive increased the enantiomeric excess of the products.[11–13] However, in our case, the yield decreased dramatically (Table 3, entries 2 and 12). In contrast to the ethylation of *E*-cinnamaldehyde **2j** in the presence of **1a**, which afforded the product in 100% ee,[16a] phenylation of **2j** resulted in only moderate selectivity, 59% ee (Table 3, entry 11).

Table 3. Phenylation reaction of aromatic aldehydes[a]



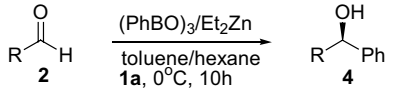
Entry	Aldehyde	R	Yield (%)[b]	ee (%)[c]
1	**2a**	*p*-Cl-phenyl	91	89
2[d]	**2a**	*p*-Cl-phenyl	37	96
3	**2b**	*m*-Cl-phenyl	87	88
4	**2c**	*o*-Cl-phenyl	90	83
5	**2d**	*p*-Br-phenyl	95	94
6	**2e**	*m*-Br-phenyl	90	73
7	**2f**	*p*-CF_3-phenyl	86	79
8	**2g**	*p*-MeO-phenyl	96	91
9	**2h**	*p*-F-phenyl	96	94
10	**2i**	2, 4-Cl, Cl-phenyl	97	83
11	**2j**	*E*-Cinnamyl	93	59
12[d]	**2j**	*E*-Cinnamyl	47	72
13	**2k**	*p*-Me-phenyl	95	87
14	**2l**	1-Naphthyl	91	93

[a] **2**/$(PhBO)_3$/Et_2Zn/**1a** = 1:0.66:4:0.1, aldehyde concentration approximately 0.1 M.
[b] Isolated yields.
[c] Determined by chiral HPLC, the configuration of **4** was determined by comparing with literature data.
[d] Using 0.1 equiv DiMPEG (MW 2000) as an additive.

Further, to optimize these reaction conditions, we found that pretreating **1a** with Et_2Zn could improve the enantioselectivity of this reaction. For substrate **2a**, the enantioselectivity increased from 89% ee (Table 3, entry 1) to 95% ee (Table 4, entry 1). Pu et al. also reported the same effect of pretreating the ligand with Et_2Zn using a chiral binol ligand.[6]

Pretreatment of **1a** with Et_2Zn could improve the enantioselectivity except for substrate **2g** (Table 3, entry 8 vs Table 4, entry 10). The best result was obtained at 0 °C for substrate **2a**, although the selectivity was slightly lower when the reaction was carried out at 15 and −15 °C, 91% ee and 93% ee, respectively (Table 4, entries 2 and 3). When the amounts of boroxin and Et_2Zn were decreased to 0.38 and 1.3 equiv, the concentration of **2a** was increased to 0.2 M with the desired alcohol **4a** being produced in 91% ee in a lower isolated yield, 62% (Table 4, entry 4). Using 0.05 equiv of **1a** afforded the diaryl methanol in 91% ee (Table 4, entry 5), which is comparable to that of using 0.1 equiv **1a**. For substrate **2j**, *E*-cinnamaldehyde, under these

Table 4. Phenylation of aldehydes with further optimized catalysis system[a]



Entry	Aldehyde	R	Temperature (°C)	Yield (%)[b]	ee (%)[c]
1	**2a**	*p*-Cl-phenyl	0	93	95
2	**2a**	*p*-Cl-phenyl	15	84	91
3	**2a**	*p*-Cl-phenyl	−15	87	93
4[d]	**2a**	*p*-Cl-phenyl	0	62	91
5[e]	**2a**	*p*-Cl-phenyl	0	93	91
6	**2b**	*m*-Cl-phenyl	0	93	95
7	**2c**	*o*-Cl-phenyl	0	89	95
8	**2e**	*m*-Br-phenyl	0	93	87
9	**2f**	*p*-CF_3-phenyl	0	81	88
10	**2g**	*p*-MeO-phenyl	0	82	90
11	**2i**	2, 4-Cl, Cl-phenyl	0	73	93
12	**2j**	*E*-Cinnamyl	0	88	83
13	**2k**	*p*-Me-phenyl	0	93	88
14	**2l**	1-Naphthyl	0	87	95
15	**2m**	2-Naphthyl	0	88	94
16	**2n**	*o*-Br-phenyl	0	91	92

[a] Concentration of aldehyde is approximately 0.1 M.
[b] Isolated yield.
[c] Ee values determined by chiral HPLC, the configuration of **4** determined by comparison with literature data.
[d] **2**/**3a**$(PhBO)_3$/Et_2Zn/**1a** = 1:0.38:1.30:0.1, the concentration of **2a** approximately 0.2M.
[e] Using 0.05 equiv ligand **1a**.

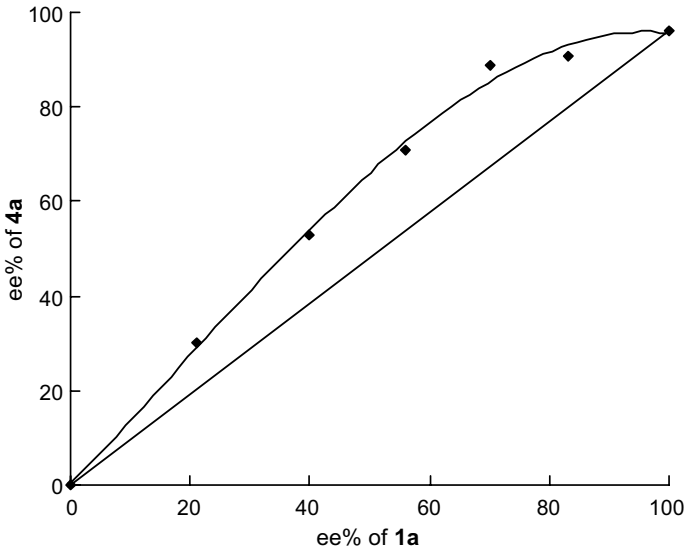
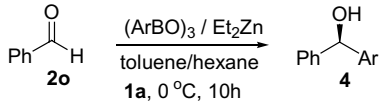


Figure 2. Nonlinear effect of amino alcohol **1a**.

reaction conditions the selectivity improved from 59% ee (Table 3, entry 11) to 83% ee (Table 4, entry 12). Benzaldehyde with an *ortho* and *meta* substituent gave comparable ee values to that of the *para* one (Table 3, entries 1, 3, and 4 and Table 4, entries 1, 6–8, and 16). 1-Naphthaldehyde and 2-naphthaldehyde afforded excellent results, 95% ee and 94% ee, respectively (Table 4, entries 14 and 15).

As shown in Figure 2, **1a** shows a weak positive nonlinear effect in the reaction between **2a** and the phenyl zinc species generated from phenylboroxin and Et_2Zn. When *p*-chlorobenzaldehyde and the zinc species are reacted in the presence of 20 mol % of **1a** in 70% ee, which is pretreated with Et_2Zn, alcohol **4a** is produced in 91% ee. This result is comparable to that of using enantiomerically pure **1a**.

Table 5. Arylation of benzaldehyde using substituted phenylboroxin[a]



Entry	Boroxin	Ar	Product	Yield (%)[b]	ee (%)[c]
1[d]	**3b**	*p*-Cl-phenyl	**4a**	89	58
2	**3b**	*p*-Cl-phenyl	**4a**	88	94
3[d]	**3c**	*p*-Me-phenyl	**4k**	82	27
4	**3c**	*p*-Me-phenyl	**4k**	97	81
5	**3d**	*p*-Br-phenyl	**4d**	91	93
6	**3e**	*m*-Br-phenyl	**4e**	84	94
7	**3f**	*p*-MeO-phenyl	**4g**	87	92

[a] As the procedure described in Table 4, **2**/**3**$(ArBO)_3$/Et_2Zn/**1a** = 1:0.67:4:0.1. The concentration of aldehyde is approximately 0.1 M.
[b] Isolated yields.
[c] Ee values determined by chiral HPLC, the configuration of **4** determined by comparison with literature data.
[d] The ligand was not pretreated with Et_2Zn.

Next, we investigated the possibility of varying the structure of the aryl source and studied the asymmetric aryl transfer from various substituted phenyl boroxin to benzaldehyde, **2o**. As shown in Table 5, pretreatment of the ligand with Et_2Zn improves the ee value greatly for boroxin **3b** (81% ee vs 27% ee) and **3c** (94% ee vs 58% ee) as compared to that of without pretreatment of Et_2Zn (Table 5, entries 1–4). *para*- and *meta*-Bromo substituted phenyl boroxin afforded the products in excellent selectivity, 93% ee and 94% ee, respectively (Table 5, entries 5 and 6). Using *p*-methoxylphenyl boroxin **3f** as the aryl source, alcohol **4g** was obtained in 92% ee (Table 5, entry 7), which was slightly higher than that of the phenyl addition of aldehyde **2g** (Table 4, entry 10).

3. Conclusion

In conclusion, different protocols for the enantioselective addition of aryl zinc species to aromatic aldehydes in the presence of amino alcohols derived from L-proline have been studied. Generally, the enantioselectivity can be improved by pretreating the amino alcohol with Et_2Zn. The phenyl groups in phenyl boroxin are transferred effectively to a variety of aromatic aldehydes in high yield and good enantioselectivity. Substituted phenyl boroxins are also used as aryl source, and transferred effectively in high ee. Although using DiMPEG as an additive can improve the ee, the yield, however, dropped greatly.

4. Experimental

General: NMR spectra were recorded at 300 MHz for ^1H, and 75 MHz for ^{13}C. Chemical shifts are reported in δ ppm referenced to an internal TMS standard for ^1H NMR and chloroform-*d* (δ 77.05) for ^{13}C NMR. The enantiomeric excess of **4a**–**n** was determined by

Chiral HPLC. THF was freshly distilled over sodium/benzophenone before use. Toluene was freshly distilled from CaH_2.

4.1. Preparation of amino alcohol 1a–h

4.1.1. Preparation of amino alcohol 1a. A solution of methyl L-1-ethoxycarbonylprolinate (8.6 g, 42 mmol) in THF (20 mL) was placed in the addition funnel and added slowly to a solution of phenyl magnesium bromide (90 mmol) at 0 °C in 20 min. After the addition, the mixture was stirred at room temperature for 0.5 h and then heated at reflux for 4 h. The mixture was cooled to room temperature, and then an ice-cold solution of saturated NH_4Cl was added. The aqueous layer was extracted with ether. The combined organic layer was dried over anhydrous Na_2SO_4. Removal of the solvent gave the crude product as a yellow solid, which was recrystallized from ethyl acetate to afford a white crystalline solid (9.3 g, 78%), which was used directly in the next step.

To a flame dried 250 mL three-necked flask was added anhydrous THF (50 mL) under an inert atmosphere of argon. LAH (2.7 g, 71 mmol) was added in three portions. A solution of the product in first step (25 mmol) in THF (30 mL) was added dropwise through a 100 mL addition funnel at 0 °C. Then the mixture was heated at reflux for 4 h. The reaction was quenched by water after being cooled to 0 °C. The mixture was acidified to pH 3 with 1 M HCl, washed with Et_2O, and made alkaline with concentrated aqueous NaOH. The precipitate was filtered off and washed with ethyl acetate. The organic layer was separated, and the filtrate extracted with CH_2Cl_2. The combined extract was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. Compound **1a** was obtained as a white crystalline solid (6.69 g, 96%) after being recrystallized from hexane. $[\alpha]_D^{20} = +59$ (c 0.77, $CHCl_3$) {lit.[16a] $[\alpha]_D^{23} = +57$(c 1.0, $CHCl_3$)}; ^{1}H NMR ($CDCl_3$) δ 7.70–7.05 (m, 10H), 4.80–4.75 (m, 1H), 3.65–3.55 (dd, 1H, J = 9.6, 3.9 Hz), 3.15–3.00 (m, 1H), 2.50–2.35 (m, 1H), 2.10–1.50 (m, 7H).

4.1.2. Preparation of ligand 1b. The compound was prepared analogously to **1a**: $[\alpha]_D^{20} = -60$ (c 0.69, $CHCl_3$) {lit.[16a] $[\alpha]_D^{23} = -57$ (c 1.00, $CHCl_3$)]; ^{1}H NMR ($CDCl_3$) δ 7.70–7.05 (m, 10H), 4.80–4.75 (m, 1H), 3.65–3.55 (dd, 1H, J = 9.6, 3.9 Hz), 3.15–3.00 (m, 1H), 2.50–2.35 (m, 1H), 2.10–1.50 (m, 7H).

4.1.3. Preparation of 1c. This compound was prepared from methyl L-1-ethoxycarbonylprolinate and the Grignard reagent prepared from 1,4-dibromobutane according to the procedure described for compound **1a**, purified by silica gel column chromatography with ethyl acetate and methanol (3:1) as a light yellow oil (81% yield). $[\alpha]_D^{20} = -49$ (c 1.36, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.70–7.05 (10H), 4.80–4.75 (m, 1H), 3.13–3.05 (m, 1H), 2.45 (s, 3H), 2.40–2.30 (m, 2H), 1.90–1.40 (m, 12H); ^{13}C NMR ($CDCl_3$) δ 82.4, 73.2, 58.8, 43.5, 40.8, 37.1, 28.7, 24.5, 23.2; IR (KBr) 3446, 2961, 2871, 2848, 2786, 1458, 1382, 1040, 1002 cm^{-1}; HRMS for $C_{12}H_{19}NO$ (M+Na)$^+$ 192.1359, found 192.1357.

4.1.4. Preparation of 1d. The compound was prepared analogously to **1a**: purified by silica gel chromatography with ethyl acetate and methanol (10:1 to 3:1), then recrystallized from hexane to give a white crystalline solid. Mp 94–96 °C; $[\alpha]_D^{20} = +19.7$ (c 2.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.51–7.47 (d, 2H, J = 8.1 Hz), 7.41–7.38 (d, 2H, J = 8.1 Hz), 4.70 (s, 1H), 3.60–3.54 (dd, 1H, J = 9.3, 3.9 Hz), 3.12–3.05 (m, 1H), 2.50–2.35 (m, 1H), 2.25 (s, 6H), 1.95–1.85 (m, 1H), 1.82 (s, 3H), 1.75–1.59 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 145.5, 144.0, 135.4, 135.3, 128.6, 125.3, 125.1, 77.1, 71.8, 59.1, 43.0, 29.8, 23.9, 20.9, 20.7; IR (KBr) 3355, 3093, 3057, 2967, 2948, 2872, 2789, 1798, 1507, 1459, 1371, 1175, 1042, 799, 778, 735 cm^{-1}; HRMS for $C_{20}H_{26}NO$ (M+H)$^+$ 296.2009, found 296.2009.

4.1.5. Preparation of 1e. The compound was prepared analogously to **1a**, then recrystallized from hexane to give a white crystalline solid. Mp 63–64 °C; $[\alpha]_D^{20} = +30.2$ (c 0.829, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.46 (s, 1H), 7.41–7.38 (d, 1H, J = 7.5 Hz), 7.36 (s, 1H), 7.31–7.28 (d, 1H, J = 7.5 Hz), 7.20–7.10 (t, 1H, J = 7.5 Hz), 6.98–6.90 (m, 2H), 4.73 (s, 1H), 3.65–3.55 (dd, 1H, J = 9.0, 5.2 Hz), 3.12–3.05 (m, 1H), 2.50–2.35 (m, 1H), 2.31 (s, 3H), 2.30 (s, 3H), 1.95–1.85 (m, 1H), 1.80 (s, 3H), 1.75–1.59 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 148.1, 146.6, 137.4, 127.6, 126.7, 126.1, 122.6, 122.3, 77.3, 71.9, 59.1, 42.9, 29.8, 23.9, 21.6; IR (KBr) 3315, 3093, 3057, 2987, 2943, 2856, 2792, 1601, 1486, 1459, 1387, 1157, 1041, 782, 770, 709 cm^{-1}; HRMS for $C_{20}H_{26}NO$ (M+H)$^+$ 296.2009, found 296.2010.

4.1.6. Preparation of 1f. The compound was prepared analogously to **1a**, and purified by silica gel column chromatography to give a colorless oil (84%), which solidified after being stored in an icebox for several days. Mp 61–62 °C; $[\alpha]_D^{20} = +30.6$ (c 1.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.50–7.10 (m, 6H), 7.00–6.85 (m, 2H), 4.85–4.60 (br, 1H), 3.65–3.55 (m, 1H), 3.15–3.05 (m, 1H), 2.50–2.35 (m, 1H), 2.31 (s, 6H), 2.00–1.50 (m, 7H); ^{13}C NMR ($CDCl_3$) δ 148.2, 146.6, 137.5, 127.6, 126.7, 126.1, 122.6, 122.3, 77.3, 71.9, 59.1, 42.9, 29.9, 23.9, 21.6; IR (KBr) 3317, 3093, 3057, 2943, 2914, 2856, 2792, 1602, 1486, 1459, 1387, 1156, 1041, 782, 770, 709 cm^{-1}; HRMS for $C_{20}H_{26}NO$ (M+H)$^+$ 296.2009, found 296.2005.

4.1.7. Preparation of 1g. The compound was prepared analogously to **1a**, then recrystallized from hexane to give a white crystalline. $[\alpha]_D^{20} = +41$ (c 1.05, $CHCl_3$) {lit.[16b] $[\alpha]_D^{20} = +40.5$ (c 1.75, $CHCl_3$)}; ^{1}H NMR ($CDCl_3$) δ 7.60–7.40 (m, 4H), 7.00–6.90 (m, 4H), 4.82 (m, 1H), 3.60–3.55 (dd, 1H, J = 11.4, 4.8 Hz), 3.15–3.08 (m, 1H), 2.50–2.40 (m, 1H), 1.95–1.55 (m, 7H).

4.1.8. Preparation of 1h. The compound was prepared according to the literature procedure.[19] $[\alpha]_D^{20} = -54.6$ (c 2.34, $CHCl_3$) {lit.[19] $[\alpha]_D^{20} = -53.5$ (c 0.26, $CHCl_3$)}; ^{1}H NMR ($CDCl_3$) δ 7.60–7.45 (m, 4H), 7.35–7.15 (m, 6H), 4.70–4.50 (br, 1H), 4.30–4.20 (t, 1H, J = 4.5Hz), 3.06–2.90 (m, 2H), 1.80–1.50 (m, 1H).

4.2. Typical procedure for the preparation of arylboroxines

Phenyl boronic acid was heated at 110 °C for 6 h in an oven; boronic acid was converted to phenyl boroxin quantitatively by this procedure. ^{1}H NMR ($CDCl_3$) δ 8.20–8.30 (m, 6H), δ 7.40–7.60 (m, 9H).

Other arylboroxines were prepared by the same procedure.

4.3. Typical procedure for the phenyl transfer reaction

A flame dried Schlenk tube was charged with phenyl boroxine (62 mg, 0.6 mmol) under an inert atmosphere (Ar). Et_2Zn (1.2 mmol, 1 M in hexane) was added via a syringe. The mixture was stirred for 10 h at 60 °C. Another Schlenk tube was then charged with **1a** (8 mg, 0.03 mmol) and freshly distilled toluene (0.5 mL) under an Ar atmosphere, and then stirred for 0.5 h at room temperature. The clear solution in the first tube was transferred to the second tube via a syringe. The resulting mixture was stirred for 0.5 h at room temperature. After the mixture was cooled to 0 °C in an ice bath, *p*-chlorobenzaldehyde **2a** (42 mg, 0.3 mmol) dissolved in toluene (1.5 mL) was added dropwise via a syringe. The whole mixture was stirred for 10 h at 0 °C. Then the reaction was quenched with 1 M HCl and extracted with ethyl acetate, the combined organic layer was washed with saturated brine and dried over anhydrous Na_2SO_4. Removal of the solvent and purification by silica gel column chromatography with ethyl acetate and hexane gave the product alcohol **4a**. Enantiomeric excess was determined by chiral HPLC.

Pretreatment of amino alcohol **1a**: To a solution of **1a** (8 mg, 0.03 mmol) in toluene was added Et_2Zn (0.06 mmol, 1 M in hexane) and stirred for 0.5 h at room temperature.

4.3.1. (*S*)-(4-Chlorophenyl)phenyl-methanol 4a.[8] The compound was obtained as a white solid; mp 54–55 °C; $[\alpha]_D^{20} = +22$ (c 0.48, $CHCl_3$) for 95% ee {lit.[8] $[\alpha]_D^{25} = -18.3$ (c 0.86, $CHCl_3$), for 94% ee (*R*)-**4a**}; ^{1}H NMR ($CDCl_3$) δ 7.40–7.25 (m, 9H), δ 5.83–5.81 (d, 1H, J = 3.3 Hz), δ 2.25–2.22 (d, 1H, J = 3.3 Hz); HPLC: Daicel Chiralcel AD column, hexane/*i*-PrOH = 9:1, 1 mL/min, λ = 254 nm, $t_R(R)$ = 10.4 min, $t_R(S)$ = 11.4 min.

4.3.2. (*S*)-(3-Chlorophenyl)phenyl-methanol 4b.[8] The compound was obtained as a colorless oil; $[\alpha]_D^{25} = +35.7$ (c 0.27, acetone) for 95% ee {lit.[8] $[\alpha]_D^{25} = -27.6$ (c 1.12, acetone), for 92% ee (*R*)-**4b**}; ^{1}H NMR ($CDCl_3$) δ 7.45–7.20 (m, 9H), δ 5.81–5.79 (d, 1H, J = 3.9 Hz), δ 2.29–2.28 (d, 1H, J = 3.9 Hz); HPLC: Daicel Chiralcel OD column, hexane/*i*-PrOH = 19:1, 0.75 mL/min, λ = 254 nm, $t_R(S)$ = 36.1 min, $t_R(R)$ = 39.7 min.

4.3.3. (*S*)-(2-Chlorophenyl)phenyl-methanol 4c.[8] The compound was obtained as a colorless oil; $[\alpha]_D^{25} = -26$ (c 0.58, $CHCl_3$) for 93% ee {lit.[8] $[\alpha]_D^{25} = 22.3$ (c 1.75, $CHCl_3$), for 96% ee (*R*)-**4c**}; ^{1}H NMR ($CDCl_3$) δ 7.63–7.59 (d, 1H, J = 7.5 Hz), δ 7.41–7.20 (m, 8H), δ 6.20–6.23 (d, 1H, J = 3.9 Hz), δ 2.42–2.39 (d, 1H, J = 3.9 Hz); HPLC: Daicel Chiralcel OD column, hexane/*i*-PrOH = 9:1, 0.75 mL/min, λ = 254 nm, $t_R(R)$ = 15.8 min, $t_R(S)$ = 19.85 min.

4.3.4. (*S*)-(4-Bromophenyl)phenyl-methanol 4d.[7a] The compound was obtained as a white solid; mp 56–58 °C; $[\alpha]_D^{25} = +18$ (c 1.08, PhH) for 94% ee {lit.[20] $[\alpha]_D^{25} = 21$ (c 0.8, PhH), for enantiomeric pure (*R*)-**4d**}; ^{1}H NMR ($CDCl_3$) δ 7.50–7.20 (m, 9H), δ 5.82–5.81 (d, 1H, J = 7.5 Hz), δ 2.23–2.19 (d, 1H, J = 3.9 Hz); HPLC: Daicel Chiralcel AD column, hexane/*i*-PrOH = 9:1, 0.75 mL/min, λ = 254 nm, $t_R(R)$ = 14.3 min, $t_R(S)$ = 15.8 min.

4.3.5. (*S*)-(3-Bromophenyl)phenyl-methanol 4e.[7a] The compound was obtained as a colorless oil; $[\alpha]_D^{25} = +25.7$ (c 0.944, $CHCl_3$) for 87% ee; ^{1}H NMR ($CDCl_3$) δ 7.57 (s, 1H), δ 7.40–7.15 (m, 8H), δ 5.81–5.78 (d, 1H, J = 3.3 Hz), δ 2.29–2.27 (d, 1H, J = 3.3 Hz); HPLC: Daicel Chiralcel OD column, hexane/*i*-PrOH = 9:1, 0.75 mL/min, λ = 254 nm, $t_R(S)$ = 28.3 min, $t_R(R)$ = 31.9 min.

4.3.6. (*S*)-(4-Trifluoromethylphenyl)phenyl-methanol 4f. The compound was obtained as a light yellow oil; $[\alpha]_D^{25} = -61.5$ (c 0.291, $CHCl_3$) for 88% ee; ^{1}H NMR ($CDCl_3$) δ 7.70–7.25 (m, 9H), δ 6.33–6.30 (d, 1H, J = 3.6 Hz), δ 2.33–2.30 (d, 1H, J = 3.6 Hz); HPLC: Daicel Chiralcel OJ column, hexane/*i*-PrOH = 9:1, 0.75 mL/min, λ = 254 nm, $t_R(R)$ = 15.6 min, $t_R(S)$ = 20.4 min.

4.3.7. (*S*)-(4-Methoxylphenyl)phenyl-methanol 4g.[8] The compound was obtained as a white solid; mp 62–63 °C; $[\alpha]_D^{25} = -14$ (c 0.627, PhH) for 91% ee {lit.[8] $[\alpha]_D^{25} = +17$ (c 2.5, PhH), for 98% ee (*R*)-**4g**}; ^{1}H NMR ($CDCl_3$) δ 7.40–7.20 (m, 7H), 6.90–6.80 (m, 2H), 5.81–5.79 (m, 1H), 3.78 (s, 3H), 2.27–2.18 (m, 1H); HPLC: Daicel Chiralcel OJ column, hexane/*i*-PrOH = 4:1, 0.75 mL/min, λ = 254 nm, t_R (*R*) = 28.8 min, $t_R(S)$ = 31.4 min.

4.3.8. (*S*)-(4-Fluorophenyl)phenyl-methanol 4h.[16b] The compound was obtained as a colorless oil; $[\alpha]_D^{25} = +5.4$ (c 0.76, $CHCl_3$) for 94% ee; ^{1}H NMR ($CDCl_3$) δ 7.40–7.28 (m, 7H), 7.06–6.95 (m, 2H), 5.86–5.83 (d, 1H, J = 3.6 Hz), δ 2.21–2.19 (d, 1H, J = 3.6 Hz); HPLC: Daicel Chiralcel OB-H column, hexane/*i*-PrOH = 4:1, 0.75 mL/min, λ = 254 nm, t_R (*R*) = 20.0 min, $t_R(S)$ = 23.6 min.

4.3.9. (*S*)-(2,4-Dichlorophenyl)phenyl-methanol 4i.[21] The compound was obtained as a colorless oil; $[\alpha]_D^{25} = -6.1$ (c 3.83, acetone) for 93% ee {lit.[21] $[\alpha]_D^{25} = +6.7$ (c 5.00, acetone) for 86% ee (*R*)-**4i**}; ^{1}H NMR ($CDCl_3$) δ 7.70–7.20 (m, 8H), 6.20–6.10 (d, 1H, J = 3.6 Hz), 2.40–2.30 (d, 1H, J = 3.6 Hz); HPLC: Daicel Chiralcel OD column, hexane/*i*-PrOH = 4:1, 0.75 mL/min, λ = 254 nm, $t_R(S)$ = 10.0 min, $t_R(R)$ = 11.3 min.

4.3.10. (*R*)-(*E*)-1,3-Diphenyl-2-propenol 4j.[9] The compound was obtained as a colorless oil; $[\alpha]_D^{25} = +30.5$ (*c* 0.33, $CHCl_3$) for 83% ee {lit.[22] $[\alpha]_D^{20} = -32.1$ (*c* 0.5, $CHCl_3$) for enantiomerically pure (*R*)-**4j**}; ^1H NMR ($CDCl_3$) δ 7.50–7.20 (m, 10H), δ 6.70–6.60 (d, 1H, $J = 15.9$ Hz), 6.40–6.30 (dd, 1H, $J = 15.9$, 6.6 Hz), 5.40–5.33 (d, 1H, $J = 5.4$ Hz), 2.25–2.15 (m, 1H); HPLC: Daicel Chiralcel OD column, hexane/*i*-PrOH = 9:1, 0.75 mL/min, $\lambda = 254$ nm, $t_R(R) = 31.1$ min, $t_R(S) = 40.8$ min.

4.3.11. (*S*)-(4-Methylphenyl)phenyl-methanol 4k.[8] The compound was obtained as a white solid; Mp 59–60 °C; $[\alpha]_D^{25} = -7.6$ (*c* 0.33, PhH) for 88% ee {lit.[8] $[\alpha]_D^{25} = +9.0$ (*c* 0.5, PhH) for 97% ee (*R*)-**4k**}; ^1H NMR ($CDCl_3$) δ 7.40–7.10 (m, 9H), 5.80–5.83 (d, 1H, $J = 3.0$ Hz), 2.33 (s, 3H), 2.20–2.15 (m, 1H); HPLC: Daicel Chiralcel OD column, hexane/*i*-PrOH = 9:1, 0.75 mL/min, $\lambda = 254$ nm, $t_R(S) = 16.6$ min, t_R (*R*) = 18.5 min.

4.3.12. (*S*)-(1-Naphthyl)phenyl-methanol 4l.[7a] The compound was obtained as a white solid; Mp 68–70 °C; $[\alpha]_D^{25} = -44$ (*c* 0.48, $CHCl_3$) for 95% ee; ^1H NMR ($CDCl_3$) δ 8.05–7.20 (m, 12H), 6.50–6.45 (d, 1H, $J = 3.6$ Hz), 2.75–2.45 (d, 1H, $J = 3.6$ Hz); HPLC: Daicel Chiralcel OD column, hexane/*i*-PrOH = 4:1, 1 mL/min, $\lambda = 254$ nm, $t_R(S) = 15.8$ min, $t_R(R) = 34.8$ min.

4.3.13. (*S*)-(2-Naphthyl)phenyl-methanol 4m.[8] The compound was obtained as a white solid; Mp 86–87 °C; $[\alpha]_D^{25} = -7.0$ (*c* 0.39, PhH) for 94% ee {lit.[8] $[\alpha]_D^{25} = +6.3$ (*c* 1.00, PhH) for 97% ee (*R*)-**4m**}; ^1H NMR ($CDCl_3$) δ 7.90–7.70 (m, 4H), 7.50–7.20 (m, 8H), 5.90–5.80 (m, 1H), 2.60–2.50 (m, 1H); HPLC: Daicel Chiralcel OD column, hexane/*i*-PrOH = 9:1, 1 mL/min, $\lambda = 254$ nm, $t_R(S) = 22.1$ min, $t_R(R) = 26.9$ min.

4.3.14. (2-Bromophenyl)phenyl-methanol 4n.[13] The compound was obtained as a colorless oil; $[\alpha]_D^{25} = -56.5$ (*c* 0.45, acetone) for 92% ee {lit.[21] $[\alpha]_D^{25} = 46.6$ (*c* 1.3, acetone) for 95% ee (*R*)-**4n**}; ^1H NMR ($CDCl_3$) δ 7.60–7.10 (m, 9H), 6.20–6.10 (d, 1H, $J = 3.0$ Hz), 2.60–2.55 (d, 1H, $J = 3.0$ Hz); HPLC: Daicel Chiralcel OD column, hexane/*i*-PrOH = 9:1, 1 mL/min, $\lambda = 254$ nm, $t_R(R) = 13.5$ min, $t_R(R) = 20.6$ min.

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