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Chiral 1,1′-Binaphthylazepine-Derived Amino Alcohol Catalyzed Asymmetric Aryl Transfer Reactions with Boroxine as Aryl Source

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ABSTRACT Using chiral 1,1′-binaphthylazepine-derived amino alcohol as catalyst, the direct addition of in situ prepared arylzinc (with triphenylboroxine as aryl source) to various aryl aldehydes can afford optically active diarylmethanols in high yields and enantioselectivities (up to 96%). *Chirality 22:159–164, 2010.*

KEY WORDS: aryl transfer reaction; boroxine; amino alcohol; diarylmethanol; aldehydes

INTRODUCTION

Chiral diarylmethanols are important precursors for many biologically active compounds.[1–6] Two general approaches for their enantioselective syntheses have been developed, either by the reduction of prochiral diaryl ketones or the stereoselective aryl transfer reactions to aromatic aldehydes. The latter seems easier to realize because of the significant difference between the hydrogen atom and the aryl group of the aldehydes. Major breakthroughs in this field were obtained by Fu,[7] and later by Bolm and others,[8] but high enantioselectivities were mostly limited to the addition of diphenylzinc to aldehydes. In 2002, Bolm and coworkers described arylzinc species formed in situ from arylboronic acids and diethylzinc, and obtained excellent enantioselectivity in the ary transfer reaction using planar-chiral ferrocene-based oxazoline ligand.[9] However, the arylboronic acid protocol demands a huge excess of diethylzinc (6–7 equiv) for the boron–zinc transmetalation due to the acidity of boronic acid. So, further improvements on this approach were focused on the amelioration of the aryl sources[10–25] and effectual ligands.[8] Triphenylboranes,[17–19] triarylborane ammonia complexes,[20] and phenylboroxines[21–23] were all found to be viable aryl sources (see Fig. 1), and triarylboroxine has recently even been applied in industry.[26]

1,1′-Binaphthylazepine-based ligands have been known since the early 1980s, and have been tested in several asymmetric processes. Since 2001 the group of Rosini and Superchi has carried out a systematic study aimed at defining the structural features of the binaphthylazepine skeleton which are responsible for their efficiency as chiral inducers, and obtained good yields and enantioselectivities in a series of asymmetric organozinc (including dialkylzinc, diphenylzinc, and alkynylzinc) additions to aromatic aldehydes.[27–31]

Also, in 2001 our group has demonstrated that the 1,1′-binaphthylazepine-derived amino alcohol ($1R_a$,2*S*,3*R*)-**1** (see Fig. 2) was an effective catalyst for the asymmetric alkynylzinc addition reaction.[32] Later ($1R_a$,2*S*,3*R*)-**1** also showed excellent enantioselectivities on the aryl transfer reaction to aldehyde when using aryl boronic acid as aryl source.[33] To reduce the necessary amount of Et_2Zn and to make this catalytic asymmetric process synthetically useful, we attempted to explore the generality of the chiral ligand ($1R_a$,2*S*,3*R*)-**1** in the catalyzed process with aryl boroxine as aryl source.

From our previous experience, the relatively rigid structure of chiral amino alcohol presumably provided a better enantio-locking of the substrate in the aryl transfer reaction.[33] The computational study of Goldfuss and Houk on the chiral inducing mechanism pointed out the crucial role of the substituent at C(O).[34] Taking into account these studies, we imagined that a further improvement in enantioselectivity could be obtained by inserting an additional phenyl group on the C(O) of the amino alcohol skeleton (($1R_a$,2*S*)-**2** in Fig. 2), which giving rise to steric interaction with both the chiral binaphthyl moiety and the substituents on the C(O), could ensure a better enantioselective control.

EXPERIMENTAL SECTION

General

All experiments were carried out under nitrogen. All solvents were distilled from standard drying agents. Commercial aldehydes reagents were freshly redistilled before

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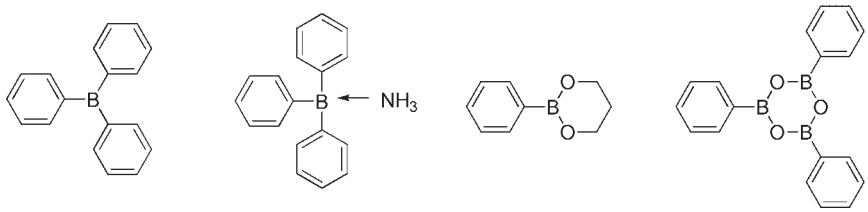
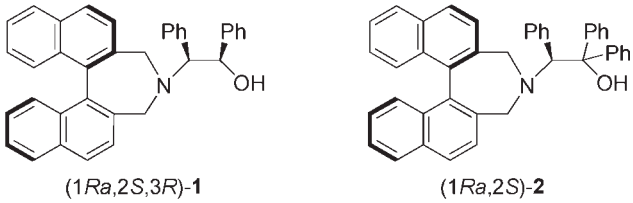


Fig. 1. Various aryl sources.

use. Crude products were purified by flash chromatography using Qing Dao Sea Chemical Reagent silica gel (200–300 mesh). NMR spectra were recorded on a Mercury Plus 300 spectrometer (Varian). Chemical shifts were reported in δ ppm referenced to an internal TMS standard for ^{1}H NMR. HPLC analyses were conducted on a Prominence LC-10A instrument (Shimadzu) using Daicel columns (0.46 cm diameter ×25 cm length). The absolute configurations of the products were determined based on the comparison of HPLC traces and/or the direction of optical rotation with known compounds.

Preparation of Chiral Amino Alcohol (1R$_a$,2S,3R)-1 and (1R$_a$,2S)-2

A solution of (1*R*,2*S*)-(+)-2-amino-1,2-diphenylethanol (0.25 mmol, 52.6 mg) in 22 mL CH_3CN was added dropwise to a flask containing 0.25 mmol (*R*)-2,2′-dibromomethyl-1,1′- binaphthyl (109.7 mg), 0.5 mmol Et_3N, and 2.0 mL toluene.[32] The mixture was stirred under reflux for 24 h and the solvent was removed. The residue obtained was dissolved in CH_2Cl_2 and the undissolved solid was removed by filtration. The filtrate was evaporated and the crude product obtained was purified via column chromatography (silica gel, petroleum ether/ethyl acetate = 120:1) to afford a white solid of (1*R$_a$*,2*S*,2*R*)-**1**, (*R*)-*N*-[(1*S*,2*R*)-1,2-diphenyl-2-hydroxyethyl]-3,5-dihydro-4*H*-dinaphtho[2,1-*c*:1′,2′-*e*]-azepine (98.7 mg, 80%). $[a]_D^{20} = -80.0$ (c 1.0, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97-7.92 (t, *J* = 8.4 Hz, 3H, ArH), 7.53-7.45 (m, 3H, ArH), 7.40-7.38 (d, *J* = 8.1 Hz, 2H, ArH), 7.31-7.28 (d, *J* = 7.8 Hz, 3H, ArH), 7.19-7.16 (m, 5H, ArH), 7.03-7.02 (d, *J* = 5.1 Hz, 4H, ArH), 6.79-6.77 (m, 3H, ArH), 5.29-5.28 (m, 1H, NCH), 4.07-4.03 (d, *J* = 12.0 Hz, 2H, CH_2N), 3.32-3.28 (d, *J* = 12.3 Hz, 2H, CH_2N). ^{13}C NMR (75 MHz, CDCl3) δ 140.9, 137.2, 135.4, 133.6, 133.3, 131.4, 129.8, 128.5, 128.4, 127.8, 127,7, 127.6, 127.5, 126.8, 126.1, 126.0, 125.7, 74.1, 72.1, 53.3. ESI-MS (m/z) for $C_{36}H_{29}NO$ $[M+H]^+$: 492.6, found 493.0, $[M+2H]^{2+}$: 493.6, found 494.0.



(1*Ra*,2*S*,3*R*)-**1** (1*Ra*,2*S*)-**2**

Fig. 2. Binaphthyl-derived amino alcohols.

Compound (1*R$_a$*,2*S*)-**2** was prepared analogously to (1*R$_a$*,2*S*,3*R*)-**1**. White solid, 86 mg, 76%. $[a]_D^{20} = -33.3$ (c 0.6, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89-7.86 (d, *J* = 8.1 Hz, 2H, ArH), 7.76-7.71 (m, 4H, ArH), 7.45-7.32 (m, 10H, ArH), 7.15-7.25 (m, 6H, ArH), 7.03-6.97 (m, 2H, ArH), 6.92-6.87 (t, *J* = 7.2 Hz, 1H, ArH), 6.56-6.53 (d, *J* = 8.4 Hz, 2H, ArH), 4.84 (s, 1H, NCH), 3.65-3.60 (d, *J* = 12.3 Hz, 2H, CH_2N), 3.36-3.31 (d, *J* = 12.3 Hz, 2H, CH_2N). ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.5, 145.5, 139.2, 135.0, 133.8, 132.9, 131.6, 131.1, 128.2, 128.1, 128.0, 127.6, 127.5, 127.3, 126.3, 125.5, 125.4, 125.3, 79.7, 76.1, 54.4. ESI-MS (m/z) for $C_{42}H_{33}NO$ $[M+H]^+$: 568.3, found 568.1.

General Procedure for the Preparation of Arylboroxines

Phenyl boronic acid was heated at 110°C for 6 h in an oven and was converted to phenyl boroxine quantitatively by this procedure.[21] ^{1}H NMR ($CDCl_3$) δ 8.20-8.30 (m, 6H), 7.40-7.60 (m, 9H). Other arylboroxines were prepared similarly.

General Procedure for the Aryl Transfer Reaction

Phenylboroxine (0.198 mmol, 61.7 mg) was mixed with diethylzinc (1 M in hexane, 1.2 mmol, 1.2 mL) in a sealed vessel and stirred for 10 h at 60°C. Another tube was charged with chiral (1*R$_a$*,2*S*,3*R*)-**1** (0.03 mmol, 14.7 mg), freshly distilled toluene (0.5 mL) and diethylzinc solution (1 M in hexane, 0.06 mmol, 0.06 mL) and stirred for 0.5 h at room temperature for the pretreatment of the ligand. Then the in situ prepared phenylzinc reagent in the first vessel was transferred to the second tube via a syringe and the resulting mixture was stirred for 0.5 h at room temperature. The tube was cooled to 0°C, and a solution of *p*-chlorobenzaldehyde (0.3 mmol, 42.2 mg) in toluene (1.5 mL) was then added dropwise and stirred for 10 h. The reaction was quenched with 1 N HCl, extracted with EtOAc (3 × 10 mL), the combined organic layer was washed with saturated brine and dried over Na_2SO_4. The crude diarylmethanol was purified by column chromatography (silica gel, EtOAc/petroleum ether = 1:20) to give the product in 87% yield and 93% ee. Enantiomeric excess was determined by chiral HPLC analysis with Chiralcel AD-H column (Daicel Chemical Industry), eluent: hexane/*i*-PrOH = 90:10, 1.0 mL/min, λ = 254 nm, $t_R(R)$ = 7.8 min, $t_R(S)$ = 8.5 min.

(*R*)-(4-Chlorophenyl)phenylmethanol[21]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40-7.21 (m, 9H, ArH), 5.79 (s, 1H,

CH). HPLC: Daicel Chiralcel AD-H, hexane/*i*-PrOH = 90:10; 1.0 mL/min, λ = 254 nm, t_R(*R*) = 7.8 min, t_R(*S*) = 8.5 min.

(*R*)-(3-Chlorophenyl)phenylmethanol[21]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32-7.16 (m, 9H, ArH), 5.71-5.70 (d, *J* = 2.7 Hz, 1H, CH). HPLC: Daicel Chiralcel OD-H, hexane/*i*-PrOH = 95:5, 0.75 mL/min, λ = 254 nm, t_R(*S*) = 23.8 min, t_R(*R*) = 26.3 min.

(*R*)-(2-Chlorophenyl)phenylmethanol[33]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63-7.60 (m, 1H, ArH), 7.38-7.23 (m, 8H, ArH), 6.20 (s, 1H, CH). HPLC: Daicel Chiralcel OD-H, hexane/*i*-PrOH = 95:5; 1.0 mL/min, λ = 254 nm, t_R(*R*) = 11.7 min, t_R(*S*) = 14.7 min.

(*R*)-(4-Methoxyphenyl)phenylmethanol[21]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39-7.26 (m, 7H, ArH), 6.88-6.85 (d, *J* = 8.7 Hz, 2H, ArH), 5.81 (s, 1H, CH), 3.80 (s, 3H, CH_3). HPLC: Daicel Chiralcel AD-H, hexane/*i*-PrOH = 90:10, 1.0 mL/min, λ = 254 nm, t_R(*R*) = 39.4 min, t_R(*S*) = 43.2 min.

(*R*)-(3-Methoxyphenyl)phenylmethanol[33]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-7.25 (m, 6H, ArH), 6.96 (m, 2H, ArH), 6.82-6.79 (d, *J* = 7.5 Hz, 1H, ArH), 5.80 (s, 1H, CH), 3.79 (s, 3H, CH_3), 2.28 (m, 1H, OH). HPLC: Daicel Chiralcel OD-H, hexane/*i*-PrOH = 95:5, 0.8 mL/min, λ = 254 nm, t_R(*S*) = 30.0 min, t_R(*R*) = 43.2 min.

(*R*)-(2-Methoxyphenyl)phenylmethanol[33]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42-7.26 (m, 7H, ArH), 6.89-6.99 (m, 2H, ArH), 6.08 (s, 1H, CH), 3.82 (s, 3H, CH_3). HPLC: Daicel Chiralcel OD-H, hexane/*i*-PrOH = 97:3, 0.8 mL/min, λ = 254 nm, t_R(*S*) = 30.4 min, t_R(*R*) = 31.7 min.

(*R*)-(4-Bromophenyl)phenylmethanol[21]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47-7.44 (d, *J* = 8.1 Hz, 2H, ArH), 7.34-7.25 (m, 7H, ArH), 5.80 (s, 1H, CH), 2.28 (s, 1H, OH). HPLC: Daicel Chiralcel AD-H, hexane/*i*-PrOH = 90:10; 0.75 mL/min, λ = 254 nm, t_R(*R*) = 11.5 min, t_R(*S*) = 13.0 min.

(*R*)-(3-Bromophenyl)phenylmethanol[21]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56-7.51 (m, 1H, ArH), 7.40-7.28 (m, 7H, ArH), 7.21-7.16 (m, 1H, ArH), 5.79 (s, 1H, CH), 2.39 (s, 1H, OH). HPLC: Daicel Chiralcel OD-H, hexane/*i*-PrOH = 90:10; 0.75 mL/min, λ = 254 nm, t_R(*S*) = 12.4 min, t_R(*R*) = 13.7 min.

(*R*)-(4-Tolyl)phenylmethanol[21]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39-7.33 (m, 4H, ArH), 7.29-7.25 (m, 3H, ArH), 7.16-7.14 (d, *J* = 7.5 Hz, 2H, ArH), 5.82 (s, 1H, CH), 2.35 (s, 3H, CH_3), 2.22 (m, 1H, OH). HPLC: Daicel Chiralcel OD-H, hexane/*i*-PrOH = 90:10; 0.75 mL/min, λ = 254 nm, t_R(*S*) = 12.0 min, t_R(*R*) = 12.8 min.

(*R*)-(3-Tolyl)phenylmethanol[24]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40-7.28 (m, 5H, ArH), 7.23-7.15 (m, 3H, ArH), 7.10-7.07 (d, *J* = 8.1 Hz, 1H, ArH), 5.81 (s, 1H, CH). HPLC: Daicel Chiralcel OB-H, hexane/*i*-PrOH = 90:10; 1.0 mL/min, λ = 254 nm, t_R(*R*) = 16.7 min, t_R(*S*) = 29.6 min.

(*R*)-(4-Trifluoromethylphenyl)phenyl-methanol[21]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60-7.58 (d, *J* = 8.1 Hz, 2H, ArH), 7.52-7.49 (d, *J* = 9.0 Hz, 2H, ArH), 7.36-7.26 (m, 5H, ArH), 5.88-5.87 (d, *J* = 2.7 Hz, 1H, CH), 2.49 (s, 1H, OH). HPLC: Daicel Chiralcel OJ-H, hexane/*i*-PrOH = 95:5, 0.75 mL/min, λ = 254 nm, t_R(*R*) = 14.7 min, t_R(*S*) = 16.3 min.

(*R*)-(1-Naphthyl)phenylmethanol[33]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05-8.02 (d, *J* = 8.7 Hz, 1H, ArH), 7.88-7.81 (m, 2H, ArH), 7.65-7.63 (d, *J* = 6.9 Hz, 1H, ArH), 7.52-7.26 (m, 8H, ArH), 6.53 (s, 1H, CH). HPLC: Daicel Chiralcel OD-H, hexane/*i*-PrOH = 90:10, 1.0 mL/min, λ = 254 nm, t_R(*S*) = 15.2 min, t_R(*R*) = 31.0 min.

(*R*)-(2-Naphthyl)phenylmethanol[33]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88-7.86 (m, 4H, ArH), 7.43-7.38 (m, 8H, ArH), 6.00 (s, 1H, CH). HPLC: Daicel Chiralcel OD-H, hexane/*i*-PrOH = 95:5, 1.0 mL/min, λ = 254 nm, t_R(*S*) = 29.3 min, t_R(*R*) = 35.9 min.

(*R*)-(2-Furyl)phenylmethanol[33]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45-7.43 (m, 2H, ArH, —CH=O), 7.41-7.31 (m, 4H, ArH), 6.33-6.31 (m, 1H, =CH-), 6.12-6.11 (d, *J* = 3.3 Hz, 1H, =CH—), 5.84-5.83 (d, *J* = 4.2 Hz, 1H, CH). HPLC: Daicel Chiralcel OD-H, hexane/*i*-PrOH = 97:3, 1.0 mL/min, λ = 254 nm, t_R(*S*) = 25.3 min, t_R(*R*) = 31.2 min.

(*S*)-(E)-1,3-Diphenyl-2-propenol[33]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46-7.27 (m, 10H, ArH), 6.72-6.67 (d, *J* = 15.9 Hz, 1H, PhCH=C*H*), 6.44-6.36 (m, 1H, PhC*H* = CH), 5.39-5.37 (d, *J* = 6.6 Hz, 1H, CH). HPLC: Daicel Chiralcel OD-H, hexane/*i*-PrOH = 80:20, 0.8 mL/min, λ = 254 nm, t_R(*S*) = 10.9 min, t_R(*R*) = 13.4 min.

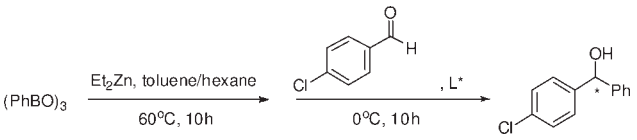
(*S*)-1-Phenyl-1-butanol[35]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27-7.18 (m, 5H, ArH), 4.61-4.58 (t, *J* = 6.6 Hz, 1H, OH), 1.83 (s, 1H, CH), 1.76-1.56 (m, 2H, CH_2), 1.40-1.18 (m, 2H, CH_2), 0.87-0.84 (t, *J* = 7.4 Hz, 3H, CH_3). HPLC: Daicel Chiralcel OB-H, hexane/*i*-PrOH = 97:3, 0.5 mL/min, λ = 254 nm, t_R(*S*) = 14.0 min, t_R(*R*) = 16.8 min.

RESULTS AND DISCUSSION

We first synthesized chiral ligands (1R_a,2*S*,3*R*)-**1** and (1R_a,2*S*)-**2**, and examined their catalytic performance in the enantioselective aryl transfer reaction of 4-chlorobenzaldehyde with phenyl boroxine as aryl source. We adopted an optimized procedure developed by Wu et al.[21] and the results were listed in Table 1. Both catalysts provided the corresponding diaryl methanols in good yields and fine ees, but (1R_a,2*S*,3*R*)-**1** showed higher efficiency, affording an ee about 6% higher than (1R_a,2*S*)-**2**. It seems that the minor structural modification on the substitute at C(O) did not provide better control of stereochemistry.

Previous studies on the aryl transfer reaction with boronic acid as the aryl source had shown that the presence of polyethers as DiMPEG could lead to a significant increase in enantioselectivity.[10] We also studied the influence of such modifiers in this new protocol, and found that at low catalyst loading (5 mol % catalyst), by the addition of 10 mol % of DiMPEG to the reaction mixture,

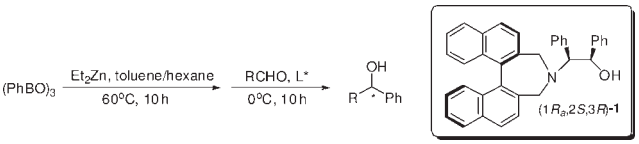
TABLE 1. Optimization of the phenylation reaction[a]



Entry	Ligand	Catalyst (mol %)	DiMPEG (mol %)	Yield (%)[b]	ee (%)[c]
1	(1R_a,2*S*,3*R*)-**1**	10	0	87	93(*R*)
2	(1R_a,2*S*)-**2**	10	0	81	87(*R*)
3	(1R_a,2*S*,3*R*)-**1**	5	0	47	44(*R*)
4	(1R_a,2*S*,3*R*)-**1**	5	10	34	94(*R*)
5	(1R_a,2*S*,3*R*)-**1**	5	25	69	56(*R*)

[a]Reaction conditions: Aldehyde/ligand/phenylboroxine/diethylzinc = 1/0.1/0.66/4 (molar ratio), toluene as solvent, 60°C, 10 h.
[b]Isolated yields.
[c]Enantiomeric excess was determined by HPLC analysis. Absolute configurations were determined by comparison of the order of peak elution from HPLC analyses with literature values.

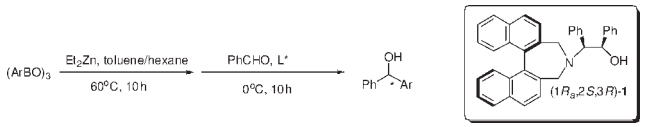
TABLE 2. Asymmetric phenyl transfer to various aldehydes[a]



Entry	Aldehyde (R=)	Yield (%)[b]	ee (%)[c]
1	*p*-chlorophenyl	87	93(*R*)
2	*p*-methoxyphenyl	80	94(*R*)
3	*p*-bromophenyl	93	93(*R*)
4	*p*-methylphenyl	87	93(*R*)
5	*p*-trifluoromethylphenyl	79	88(*R*)
6	*m*-bromophenyl	81	94(*R*)
7	*m*-chlorophenyl	75	95(*R*)
8	*m*-methoxyphenyl	85	95(*R*)
9	*o*-chlorophenyl	87	94(*R*)
10	*o*-methoxyphenyl	84	94(*R*)
11	1-naphthyl	84	96(*R*)
12	2-naphthyl	87	89(*R*)
13	2-furyl	86	81(*R*)
14	(*E*)-cinnamyl	70	82(*S*)
15	n-propyl	64	65(*S*)

[a]Conditions: Aldehyde/(1R_a,2*S*,3*R*)-**1**/phenylboroxin/diethylzinc = 1/0.1/0.66/4 (molar ratio), toluene as solvent, 60°C, 10 h.
[b]Isolated yields.
[c]Enantiomeric excess was determined by HPLC analysis. Absolute configurations were determined by comparison of the order of peak elution from HPLC analyses with literature values.

TABLE 3. Asymmetric aryl transfer to benzaldehyde[a]



Entry	Ar in boroxine	Yield (%)[b]	ee (%)[c]
1	*p*-chlorophenyl	85	78(*S*)
2	*p*-methylphenyl	98	94(*S*)
3	1-naphthyl	90	88(*S*)
4	2-naphthyl	87	91(*S*)
5	*m*-methylphenyl	37	rac
6	*m*-chlorophenyl	84	71(*S*)

[a]Conditions: Aldehyde/(1R_a,2*S*,3*R*)-**1**/arylboroxine/diethylzinc = 1/0.1/0.66/4 (molar ratio), toluene as solvent, 60°C, 10h.
[b]Isolated yields.
[c]Enantiomeric excess was determined by HPLC analysis. Absolute configurations were determined by comparison of the order of peak elution from HPLC analyses with literature values.

although high ee value (up to 94%) was obtained, the yield was low. A similar phenomenon was also observed with a proline-derived amino alcohol catalyst.[21] We assumed that the addition of PEG ethers would suppress some unwanted nonasymmetric pathways by deactivating the achiral metal catalysts and prevent their nonenantioselective contribution on the overall process.[10]

We then investigated the phenyl transfer reaction for a variety of aromatic aldehydes under the optimal conditions (Table 2). The reaction generally proceeded well with up to 96% ee. The scope of substrate was not limited to *para*-substituted aromatic aldehydes, the *meta*- or *ortho*- substituted substrates also afforded the corresponding products with good yields and excellent ees. Electronic effects were not significant, both electron-withdrawing substituent and electron-donating group giving comparable results. A useful intermediate for the antihistamine neobenodine could be obtained by the phenyl addition to *para*-tolualdehyde in considerable high yield (87%) and 93% ee (Entry 4). Aromatic aldehydes possessing steric hindrance, such as 1-naphthaldehdye and 2-naphthaldehyde, also proved to be suitable substrates for the asymmetric phenylation reaction (Entries 11 and 12). The in situ prepared phenylzinc reagents also worked well for the phenyl addition to 2-furaldehydes, and α,β-unsaturated *trans*-cinnamyl aldehydes, giving products with good ees (Entries 13 and 14). But for aliphatic aldehyde substrate as *n*-butylaldehyde, both yield and stereoselectivity were moderate and some side product existed (Entry 15).

Besides phenylzinc, various arylzinc reagents could also be easily transferred to aldehydes by using different substituted phenylboroxine as aryl source (Table 3). We found that the reaction was rather sensitive to the electronic effect of arylboroxines. The presence of an electron-donating group in the arylboroxine greatly facilitated the addition process to give high ee (up to 94% for 4-methylphenylboroxine versus 78% for 4-chlorophenylboroxine). Steric hindrance around the boron atom retarded the rate of reaction and lowered both yield and enantioselectivity. The use of 3-methylphenylboroxine afforded the product in 37% yield and nearly racemic form (Entry 5), while 3-chlorophenylboroxine produced the product in 84% yield

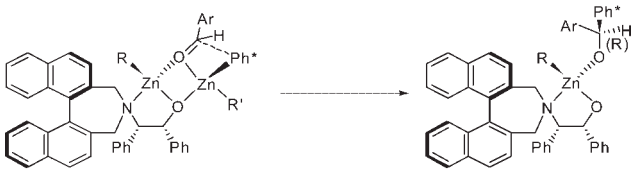


Fig. 3. The possible transition state of the phenylation.

and 71% ee (Entry 6). The presence of a bulky *meta* methyl substitute on the aryl ring showed a detrimental effect on the selectivity albeit 3-methyl was also an electron-donating group.

This methodology was quite flexible for the synthesis of diaryl methanols. With appropriate combinations of arylboroxine and aromatic aldehydes, a diverse array of oppositely configured chiral diaryl methanols can be obtained (Entry 4 of Table 2 versus Entry 2 of Table 3).

Possible transition states of the phenyl transfer step were similar to ethylation and alkynylation.[29,31,32] The stereoselective phenylation of aldehydes was promoted by the chelated phenylzinc alkoxide, which coordinated with both the carbonyl compound and a second molecule of phenylzinc reagent (see Fig. 3). The migration of the phenyl moiety to the carbonyl then occurred through a tricyclic transition state. With ligand (1R_a,2*S*,3*R*)-**1**, the phenyl group on zinc(Ph*, with the relevant phenyl ring tilting up) forced the aryl ring of the coordinated aryl aldehyde to take a position away from Ph*, consequently the phenyl transferred on the *Re* face of the carbonyl to afford predominant product with (*R*)-configuration.

In conclusion, we have demonstrated that 1,1′-binaphthylazepine-derived amino alcohol (1R_a,2*S*,3*R*)-**1** is a good catalyst for the asymmetric aryl transfer reaction with boroxines as the aryl source. Various enantiopure diarylmethanols were obtained directly altering the structures of substrates and nucleophiles. These results compared favorably with other known amino alcohol ligands in similar reaction.

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