Supporting Information for *Angew. Chem. Int. Ed.*

Engineering the Catalysts for Enantioselective Addition of Diethylzinc to Aldehydes with Racemic Amino Alcohols: Nonlinear Effect in Asymmetric Deactivation of Racemic Catalysts

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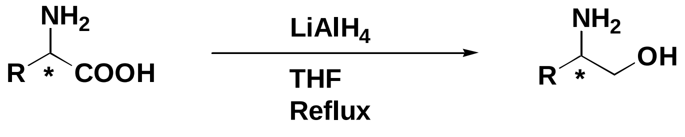
General Considerations. ^{1}H NMR spectra were measured on a Bruker AM300 NMR spectrometer (300 MHz) with $CDCl_3$ as solvent and recorded in ppm relative to internal tetramethylsilane standard. Coupling constants, *J*, are listed in hertz. Mass spectra (EI, 70 ev) were taken on a HP5989A spectrometer. Elemental analysis was preformed with an Elemental VARIO EL apparatus. Melting points are uncorrected. Optical rotations were measured on a Perkin-Elmer 341 automatic polarimeter. HPLC analyses were carried out on a JASCO 1580 liquid chromatograph with a JASCO CD-1595 detector and AS-1555 autosampler. GC analyses were performed on a Perkin-Elmer AutoSystem XL gas chromatograph with FID detection. Hexane, tetrahydrofuran and diethyl ether were distilled from sodium benzophenone ketyl under argon and degassed before use. Dichloromethane was distilled from CaH_2 before use. All reactions were performed under argon.

Preparation and Characterization of Chiral Additives (AA1-AA13) and Racemic Amino Alcohols (DB1-DB5).

Scheme 1



AA1-AA7

(*S*)-2-Amino-1-propanol (L-alaninol) (AA1)

A 50-mL round-bottomed flask was charged with a suspension of lithium aluminum hydride (0.34 g, 9 mmol) in 10 mL of dry tetrahydrofuran. The mixture was cooled to 0 ^{o}C in an ice bath and L-alanine (4.5 mmol) was added in portions during 1 h. After the addition was complete, the ice bath was removed, the reaction mixture was warmed to room temperature and stirred under reflux for 17 h. The reaction mixture was then cooled to 0^{o}C in an ice bath again and diluted with diethyl ether (10 mL). The reaction was quenched with water (0.3 mL), aqueous 15 % sodium hydroxide (0.3 mL) and water (1.0 mL) respectively. The solution was stirred for 30 min and the white precipitate was filtered through celite. The filter cake was washed with diethyl ether (3×10 mL) and the filtrates are combined, dried over anhydrous sodium sulfate and concentrated under reduced pressure to afford **AA1** (300 mg, 88%) as a colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.04 (d, 3H, J = 6.5 Hz), 2.65 (bs, 1H), 2.95-3.05 (m, 1H), 3.21-3.27 (m, 1H), 3.50-3.55 (m, 1H).

Chiral additives **AA2**-**AA7** were prepared from the corresponding amino acids by a similar procedure to that described above.

(*S*)-2-Amino-3-methyl-1-butanol (L-valinol) (AA2)
Yield: 100%; $[\alpha]_D^{25}$ + 14.4 (c = 0.51, EtOH; literature:[1] $[\alpha]_D^{21}$ + 17 (c = 10, ethanol)); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.91 (d, 3H, J = 6.8 Hz), 0.93 (d, 3H, J = 6.8 Hz), 1.53-1.65 (m, 1H) 2.27 (bs, 3H), 2.54-2.60 (m, 1H), 3.28-3.34 (m, 1H),3.62-3.67 (m, 1H).

(*S*)-2-Amino-4-methyl-1-pentanol (L-leucinol) (AA3)
Yield: 100%; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.88-0.94 (m, 6H), 1.16-1.22 (m, 2H), 1.63-1.75 (m, 1H) 2.36 (bs, 3H), 2.88-2.93 (m, 1H), 3.21-3.28 (m, 1H), 3.54-3.59 (m, 1H).

(*S*)-2-Amino-3,3-dimethyl-1-butanol (L-*tert*-leucinol) (AA4)
Yield: 98%; m.p. 34-36^{o}C (literature:[1] 33-35 ^{o}C); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.90 (s, 9H), 2.72 (bs, 3H), 3.10-3.22 (m, 1H), 3.53-3.80 (m, 2H).

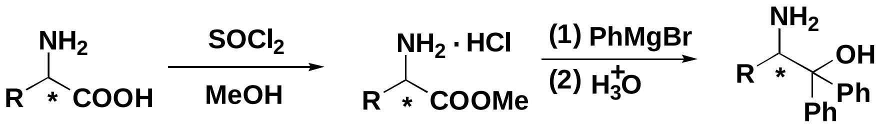
(*R*)-2-Amino-2-phenylethanol (D-phenylglycinol) (AA5)
Yield: 90%; m.p. 74-75^{o}C (literature:[1] 75-77^{o}C); $[\alpha]_D^{25}$ –35.0 (c = 1.0, 1 N HCl; literature: [1] $[\alpha]_D^{20}$ –31.70 (c = 0.76, 1 N HCl)); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 2.29 (bs, 3H),

3.52-3.58 (m, 1H), 3.70-3.75 (m, 1H), 4.01-4.06 (m, 1H), 7.26-7.36 (m, 5H).

(*S*)-2-Amino-3-phenyl-1-propanol (L-phenylalaninol) (AA6)
Yield: 92%; m.p. 88-90°C (literature:[1] 92-94°C); $[\alpha]_D^{25}$ –24.6 (c = 0.334, EtOH; literature:[2] $[\alpha]_D^{20}$ – 25.6 (c = 1.037, EtOH)); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 2.19 (bs, 3H), 2.48-2.56 (m, 1H), 2.76-2.82 (m, 1H), 3.07-3.15 (m, 1H), 3.36-3.42 (m, 1H), 3.61-3.65 (m, 1H) 7.17-7.36 (m, 5H).

(*S*)-2-Pyrrolidinemethanol (L-prolinol) (AA7)
Yield: 94%; $[\alpha]_D^{25}$ + 22.5 (c = 0.325, $C_6H_5CH_3$; literature:[3] $[\alpha]_D^{20}$ + 30 (c = 1.6, $C_6H_5CH_3$)); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.30-1.45 (m, 1H), 1.70-1.88 (m, 3H), 2.90 (t, 3H, J = 6.7 Hz), 3.20-3.29 (m, 1H), 3.36-3.39 (m, 1H), 3.53-3.62 (m, 1H).

Scheme 2



AA8-AA13

(*S*)-2-Amino-1,1-diphenyl-1-propanol (AA8)

(a) L-Alanine methyl ester hydrochloride

To a 50-mL dry 2-necked round-bottomed flask equipped with a dropping funnel and a condenser were added L-alanine (1.0 g, 11.2 mmol) and 25 mL of absolute methanol, and then the flask was immersed in an ice-bath. Thionyl chloride (0.9 mL, 12 mmol) was added dropwise under stirring during half an hour. The mixture was warmed to room temperature gradually and heated to 40-50°C for 3 h. After standing overnight at room temperature, the mixture was concentrated to give L-alanine methyl ester hydrochloride (1.6 g, 100 %) as a white crystalline solid, m.p. 108-109°C (literature:[1] 109-111°C).

(b) (*S*)-2-Amino-1, 1-diphenyl-1-propanol (AA8)

A 500-mL dry 3-necked round-bottomed flask was equipped with a dropping funnel, a condenser and an argon-inlet tube from which the flask was flushed with argon. Magnesium (2.1g, 89 mmol) and a catalytic amount of iodine were added and then about 1/5 of a solution of bromobenzene (14.7 g, 94 mmol) in 90 mL dry THF was charged to initiate the reaction followed by dropwise adding the rest solution over 1h. After the reaction mixture was stirred under reflux for 30 min, the flask was cooled to 0°C in an ice bath. L-

Alanine methyl ester hydrochloride (0.84 g, 6 mmol) was added portionwise during 1h. The mixture was stirred overnight at room temperature before it was carefully quenched with saturated ammonium chloride solution (70 mL) and extracted with ethyl acetate (4×40 mL). The organic layers were combined, dried ($MgSO_4$), filtered and concentrated. The residue was chromatographed on silica gel (EtOAc/hexane, 1:1) to yield **AA8** (1.2g, 88%) as a white solid, m.p. 99-101^{o}C (literature:[4] 101.5-102.5^{o}C); $[\alpha]_D^{25}$ – 95.2 (c = 1.0, $CHCl_3$; literature:[4] $[\alpha]_D^{25}$ – 82.3 (c = 1.6776, $CHCl_3$)); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.95 (d, 3H, J = 6.3 Hz), 1.20-1.70 (bs, 2H), 2.16 (s, 1H), 4.14 (q, 1H, J = 6.3 Hz), 7.15-7.62 (m, 10H).

Chiral additives **AA9-AA13** were prepared by using an analogous procedure as for the preparation of **AA8**.

(*S*)-2-Amino-1, 1-diphenyl-3-methyl-1-butanol (AA9)
M.p. 94-96 ^{o}C (literature:[5] 94-95^{o}C); $[\alpha]_D^{25}$ – 117.1 (c = 1.0, $CHCl_3$; literature:[5] $[\alpha]_D^{25}$ – 127.7 (c = 0.639, $CHCl_3$)); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.92-0.95 (m, 6H), 1.05-1.72 (bs, 2H), 1.75-1.88 (m, 1H), 3.91 (d, 1H, J = 1.6 Hz), 7.14-7.61 (m, 10H).

(*S*)-2-Amino-1, 1-diphenyl-4-methyl-1-pentanol (AA10)
M.p. 137-139^{o}C (literature:[6] 132-134^{o}C); $[\alpha]_D^{25}$ – 81.3 (c = 1.0, $CHCl_3$; literature:[6] $[a]_D^{25}$ – 95.12 (c = 1.006, $CHCl_3$)); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.85-0.90 (m, 6H), 1.03-1.12 (m, 1H), 1.22-1.31 (m, 1H), 1.25-1.70 (bs, 2H), 1.54-1.61 (m, 1H), 3.99 (dd, 1H, J = 2.0, 10.2 Hz), 7.18-7.62 (m, 10H).

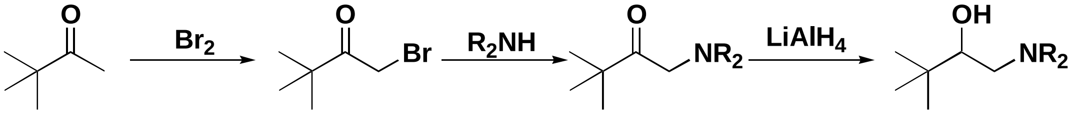
(*R*)-2-Amino-1,1,2-triphenylethanol (AA11)
Yield: 46%; m.p. 129-131 ^{o}C (literature:[7] 131-133 ^{o}C); $[\ ]_D^{25}$ + 219.1 (c = 1.0, $CHCl_3$; literature:[7] $[\ ]_D^{22}$ + 235.0 (c = 1.0, $CHCl_3$)); ^{1}H NMR (300 MHz, $CDCl_3$) = 4.75 (bs, 1H), 5.01 (s, 1H), 7.01-7.77 (m, 15H).

(*S*)-2-Amino-1,1,3-triphenyl-1-propanol (AA12)
Yield: 76%; m.p. 148-150^{o}C (literature:[6] 144-145^{o}C); $[\alpha]_D^{25}$ – 87.4 (1.0, $CHCl_3$; literature:[6] $[\alpha]_D^{25}$ – 88.50 (c = 0.604, $CHCl_3$)); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.33 (m, 2H), 2.40-2.49 (m, 1H), 2.62-2.68 (m, 1H), 4.17 (dd, 1H, J = 2.6, 10.8 Hz), 7.17-7.67 (m, 15H).

(*S*)-Diphenyl-2-pyrrolidinemethanol (AA13)

Yield: 35%; M.p. 69-71^{o}C (literature:[8] 76.5-77.5 ^{o}C); $[\alpha]_D^{25}$ – 48.2 (c = 1.0, MeOH); literature:[8] $[\alpha]_D^{21}$ – 54.3 (c = 0.261, MeOH)); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.57-1.77 (m, 4H), 2.90-3.04 (m, 2H), 4.26 (t, 1H, J = 7.7 Hz), 7.13-7.59 (m, 10H).

Scheme 3



(¡À)- DB1-DB5

(±)-1-Piperidino-3,3-dimethyl-2-butanol (DB1)

(a) 1-Bromopinacolone

A 250-mL 3-necked round-bottomed flask equipped with a dropping funnel, a condenser and a gas-outlet tube from which the evolved HBr was introduced to a NaOH solution was charged with a solution of pinacolone (20 g, 0.2 mol) in chloroform (100 mL). Bromine (32 g, 0.2 mol) was added dropwise at room temperature during 1 h. After the reaction mixture was stirred at room temperature overnight, it was transferred to a separatory funnel and washed with saturated sodium bicarbonate solution (2×50 mL) and brine (50 mL) respectively. The organic layer was dried ($MgSO_4$) filtered, and concentrated to yield 1-bromopinacolone as a colorless liquid (33.7 g, 94 %). ^{1}H NMR (90 MHz, $CDCl_3$) δ = 0.9 (s, 9H), 3.8 (s, 2H).

(b) 1-Piperidino-3,3-dimethyl-2-butanone

To a 500-mL round-bottomed flask equipped with a condenser were added 1-bromopinacolone (12 g, 67 mmol), piperidine (6 g, 70 mmol), anhydrous potassium carbonate (18.5 g, 134 mmol) and 250 mL of acetonitrile. The mixture was stirred under reflux for 20 h and then was cooled to room temperature. After water (100 mL) and ethyl acetate (100 mL) were added, the organic layer was separated, washed with brine (50 mL), dried over anhydrous sodium sulfate and concentrated under reduced pressure. Distillation of the residue under vacuum afforded 1-piperidino-3,3-dimethyl-2-butanone as a colorless liquid (6.2 g, 52 %), b.p. 76-78^{o}C /5 mmHg (Literature:[9] 90^{o}C /10 mmHg); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.13 (s, 9H), 1.37-1.45 (m, 2H), 1.57-1.64 (m, 4H), 2.40 (t, 4H), 3.31 (s, 2H).

(c) (±)-1-Piperidino-3,3-dimethyl-2-butanol (DB1)

To a 500-mL round-bottomed flask equipped with a dropping funnel were added lithium aluminum hydride (1.3 g, 34.2 mmol) and 150 mL of absolute diethyl ether. A solution of 1-piperidino-3,3-dimethyl-2-butanone (6.0 g, 32.8 mmol) in 50 mL of diethyl ether was added dropwise during half an hour. The reaction mixture was stirred at room temperature for 5 h and then diluted with diethyl ether (100 mL). The reaction mixture was quenched with water (5 mL), 15 % NaOH solution (5 mL) and water (10 mL) respectively and was filtered. The organic layer was dried over anhydrous Na_2SO_4, concentrated and chromatographed on silica gel to give racemic **DB1** (5.2 g, 85 %) as a colorless liquid. ^1H NMR (300 MHz, $CDCl_3$) $\delta = 0.89$ (s, 9H), 1.43-1.45 (m, 2H), 1.54-1.57 (m, 4H), 2.23-2.32 (m, 4H), 2.58-2.63 (m, 2H), 3.30-3.34 (m, 1H), 3.35-3.65 (bs, 1H).

Racemic amino alcohols **DB2-DB5** were prepared by using an analogous procedure as for the preparation of **DB1**.

1-(*cis*-2,6-Dimethylpiperidino)-3,3-dimethyl-2-butanol (DB2)

Yield: 85 %; ^1H NMR (300 MHz, $CDCl_3$) $\delta = 0.90$ (s, 9 H), 1.01-1.03 (m, 6H), 1.15-1.70 (m, 6H), 2.39-2.60 (m, 4H), 3.12-3.17 (m, 1H), 4.30 (bs, 1H).

1-Morpholino-3,3-dimethyl-2-butanol (DB3)

Yield: 81 %; m.p. 43-45°C (literature:[10] m.p. 49-50°C); ^1H NMR (300 MHz, $CDCl_3$) $\delta = 0.91$ (s, 9H), 2.30-2.37 (m, 4H), 2.65-2.72 (m, 2H), 3.34-3.40 (m, 1H), 3.68-3.75 (m, 4H).

1-Pyrrolidino-3,3-dimethyl-2-butanol (DB4)

Yield: 95 %; ^1H NMR (300 MHz, $CDCl_3$) $\delta = 0.91$ (s, 9 H), 1.73-1.78 (m, 4H), 2.22-2.28 (dd, 1H, $J = 2.9, 11.6$ Hz), 2.38-2.46 (m, 2H), 2.58-2.76 (m, 3H), 3.29-3.34 (dd, 1H, $J = 3.0, 11.2$ Hz).

1-(Dicyclohexyl)amino-3,3-dimethyl-2-butanol (DB5)

Yield: 76 %, m.p. 88-89°C; ^1H NMR (300 MHz, $CDCl_3$) $\delta = 0.92$ (s, 9H), 1.08-1.40 (m, 10H), 1.57-1.85 (m, 10H), 2.28-2.36 (m, 1H), 2.45-2.68 (m, 3H), 3.16 (dd, 1H, $J = 3.7, 10.8$ HZ); MS (EI, 70ev): *m/z* (%): 282 (2) $[M+1]^+$, 224 (17) $[M-C(CH_3)_3]^+$, 194 (100) $[M-HOCHC(CH_3)_3]^+$. Anal. calcd for $C_{18}H_{35}NO$: C 76.81, H 12.53, N 4.98%. Found: C 76.71, H 12.52, N 4.76.

Resolution of (±)-1-Piperidino-3,3-dimethyl-2-butanol (DB1)[11]

Both *R*-**DB1** and *S*-**DB1** can be resolved by using equimolar di-*p*-toluoyl-L-tartaric acid and di-*p*-toluoyl-D-tartaric acid respectively. Recrystallization of corresponding salts from *i*-PrOH/MeOH (3:1) mixed solvent for three times and followed by decomposition with 1 M sodium hydroxide solution gave optically pure *R*-**DB1** and *S*-**DB1** respectively in 7% yield.

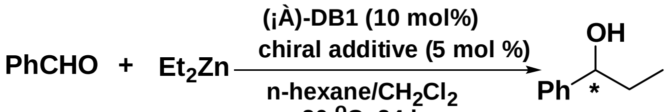
R-**DB1**: $[\alpha]_D^{25}$ = - 61.0 (C = 1.0, EtOH; literature:[12] $[\alpha]_D^{25}$ = - 62.1 (C = 1.9, EtOH))

S-**DB1**: $[\alpha]_D^{25}$ = + 61.0 (C = 1.0, EtOH)

General Procedure for the Random Screening of Chiral Additives Using Racemic 1-Piperidino-3,3-dimethyl-2-butanol (DB1) as the Ligand of Catalyst.

To a 1.5-mL polypropylene microtube were added **DB1** (3.7 mg, 0.02 mmol), chiral additives (0.01 mmol), methylene dichloride (0.1 mL) and diethylzinc (0.5 mL, 1.0 M in n-hexane) respectively. After standing at –20 °C for 24 h, the reaction mixture was quenched with saturated ammonium chloride solution and extracted with diethyl ether. The organic phase was washed with brine and dried over anhydrous sodium sulfate. After removal of the solvent, the crude product was purified by flash chromatography on silica gel with EtOAc/Hexane (1/7) as eluent to give 1-phenyl-1-propanol as a colorless liquid. Its enantiomeric excess was determined with HPLC on Chiralcel OD-H column: eluent Hexane/2-propanol (98.5:1.5); flow rate 1.0 mL/min; UV detection at λ = 270 nm; retention time = 15.0 min (R enantiomer), 20.2 min (S enantiomer).

Scheme 4



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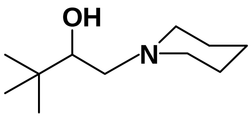
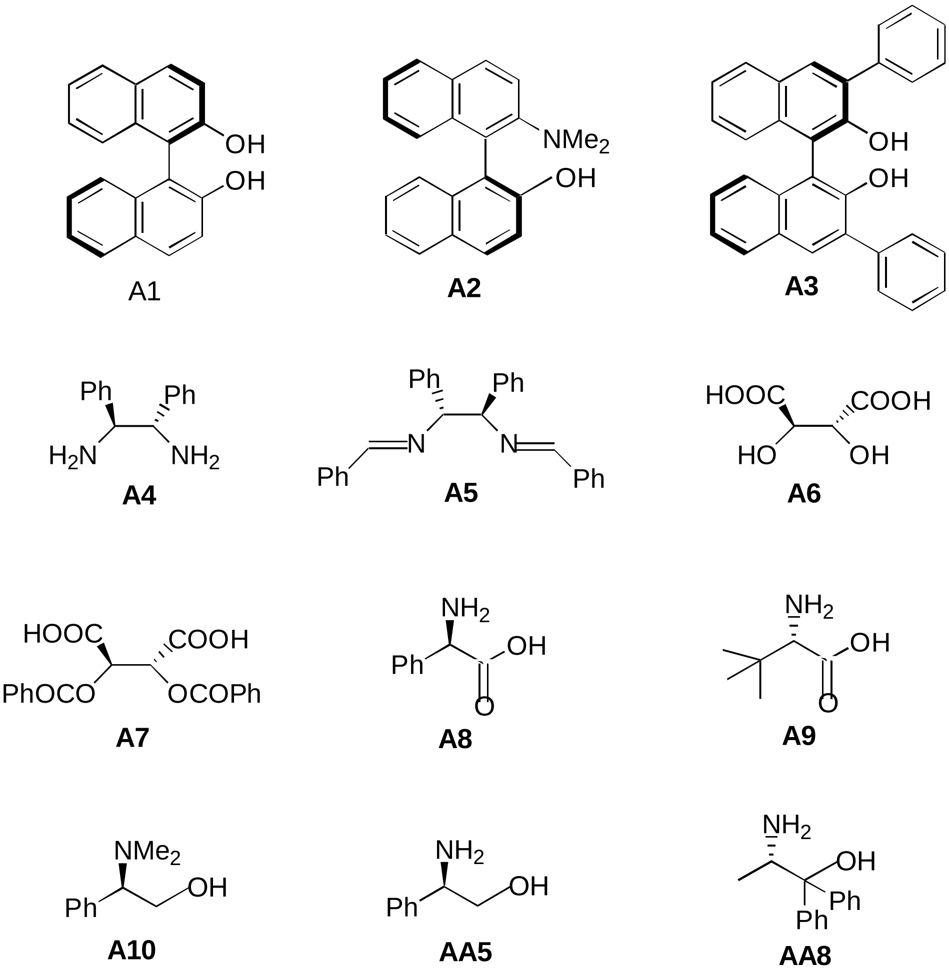


(¡À)- DB1

Table 1. Random Screening of Chiral Additives in the Presence or Absence of (±)-**DB1** as Ligand

Chiral Additives	Yield (%)		ee %	
	Without (±)-**DB1**	With (±)-**DB1**	Without (±)-**DB1**	With (±)-**DB1**
A1	54	45	8.2 (*R*)	8.5 (*S*)
A2	70	60	89.0 (*S*)	38.1 (*R*)
A3	32	85	21.1 (*R*)	0
A4	56	96	22.0 (*S*)	2.0 (*R*)
A5	64	67	1.1 (*S*)	0
A6	10	24	13.0 (*S*)	15.0 (*S*)
A7	13	70	11.0 (*R*)	13.0 (*S*)
A8	49	81	6.0 (*R*)	0
A9	15	64	0	4.0 (*R*)
A10	58	76	37.0 (*S*)	12.0 (*S*)
AA5	44	74	50.0 (*S*)	6.0 (*R*)
AA8	85	79	16.0 (*S*)	61.0 (*S*)

Scheme 5



General Procedure for High Thoughput Screening of Chiral Additives (AA) and Racemic Amino Alcohols (DB).

The high thoughput screening was carried out in a block apparatus (with a 24-well plate). Weighed amount of chiral ligands **AA** (50μL, 0.1 M in CH_2Cl_2) and racemic catalysts **DB** (50 L, 0.2 M in CH_2Cl_2) were introduced into 1.5-mL polypropylene microtubes. After diethylzinc (0.3 mL, 1.0 M in n-hexane) was introduced, the microtubes were set up in the block apparatus to keep the temperature at 0^{o}C for 30 min and finally benzaldehyde (11μL, 0.1 mmol) was added. Before the reaction mixtures were kept at 0^{o}C for 24 h, they were quenched by saturated ammonium chloride solution and extracted with n-hexane. The extracts were then submitted to HPLC-CD analysis. The results were listed in Table 2-4.

Table 2. High Throughput Evaluation of Chiral Catalyst Library Composed of Racemic Amino Alcohols (**DB**) and Optically Active Additives (**AA**).[a]

DB **AA**	**DB0**[b]	**DB1**	**DB2**	**DB3**	**DB4**	**DB5**
AA1	30.8 (*R*)	0.9 (*S*)	3.2 (*S*)	4.3 (*R*)	1.0 (*R*)	1.5 (*S*)
AA2	0	2.0 (*S*)	2.2 (*R*)	4.5 (*R*)	4.2 (*R*)	0.7 (*S*)
AA3	17.3 (*R*)	7.6 (*R*)	10.0 (*R*)	8.0 (*R*)	6.8 (*R*)	1.0 (*S*)
AA4	0	9.1 (*S*)	3.3 (*S*)	4.4 (*S*)	6.7 (*S*)	1.0 (*S*)
AA5	0	15.0 (*R*)	16.7 (*R*)	14.0 (*R*)	13.4 (*R*)	4.5 (*R*)
AA6	35.4 (*R*)	1.3 (*S*)	0.8 (*S*)	2.1 (*R*)	1.1 (*R*)	0
AA7	41.6 (*R*)	2.4 (*R*)	2.4 (*R*)	1.9 (*R*)	1.6 (*R*)	1.8 (*S*)
AA8	6.5 (*S*)	44.3 (*S*)	38.3 (*S*)	27.7 (*S*)	2.6 (*S*)	14.9 (*S*)
AA9	33.8 (*R*)	35.5 (*S*)	36.7 (*S*)	19.5 (*S*)	4.8 (*S*)	7.1 (*S*)
AA10	43.7 (*S*)	**71.1** (*S*)	**71.2** (*S*)	47.8 (*S*)	20.9 (*S*)	26.2 (*S*)
AA11	36.9 (*R*)	8.7 (*R*)	5.6 (*R*)	9.2 (*R*)	4.5 (*R*)	1.4 (*S*)
AA12	52.8 (*S*)	**69.7** (S)	**60.3** (*S*)	39.0 (*S*)	29.8 (*S*)	39.6 (*S*)
AA13	15.6 (*R*)	**65.9** (*S*)	**70.4** (*S*)	51.2 (*S*)	28.9 (*S*)	43.7 (*S*)

a. The reactions were carried out at 0^{o}C; b. **DB0** means the reaction was carried out in the absence of **DB**.

Table 3. Optimization of the Molar Ratios of Racemic Ligands (**DB**) to Chiral Additives (**AA**) [a] at different temperature.

	DB1				**DB2**			
DB/AA	0.5:1	1:1	2:1	3:1	0.5:1	1:1	2:1	3:1
AA10[b]	55.6	71.4	70.5	69.9	75.1	70.2	77.3	79.2
AA12[b]	71.4	74.9	81.7	77.6	82.1	79.0	85.3	81.8
AA13[b]	54.0	56.5	74.7	77.1	64.6	77.0	79.5	84.8
AA10[c]	76.9	82.4	80.1	81.9	78.8	81.5	78.5	79.6
AA12[c]	75.2	79.9	**83.9**	79.7	86.3	82.3	**84.0**	82.7
AA13[c]	59.5	75.5	**84.4**	81.5	83.9	85.5	**88.2**	86.9

a. The absolute configuration of 1-phenyl-1-propanol was *S*; b. The reactions were carried out at 0 °C; c. The reactions were carried out at -20 °C.

Table 4. Optimization of the Reaction Temperature.[a, b, c]

DB **AA**	**DB1**	**DB2**
AA12	86.0	86.1
AA13	92.7	90.6

a. The reactions were carried out at –40 °C; b. The molar ratio of racemic catalysts **DB** to chiral additives **AA** was 2:1; c. The absolute configuration of 1-phenyl-1-propanol was *S.*

From Table 3 and Table 4, the best reaction conditions were optimized. Then, the four combinations of ligands (**AA12/DB1**, **AA12/DB2**, **AA13/DB1** and **AA13/DB2**) were utilized to catalyze ethylation of a variety of aldehydes at –40 °C in the block apparatus and the separated secondary alcohols were submitted to chiral HPLC analysis (the results were shown in the Table 1 of the text). The absolute configurations of secondary alcohols were determined by comparing the optical rotations with that reported in literatures. The ^{1}H NMR spectra and HPLC conditions for various products were shown below.

1-Phenyl-1-propanol (2a)

^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.92 (t, 3H, J = 7.8 Hz), 1.65-1.84 (m, 2H), 1.88 (bs, 1H), 4.58 (t, 1H, J = 7.5 Hz), 7.23-7.38 (m, 5H); Chiralcel OD-H column with hexane/2-propanol (98.5:1.5) as eluent; flow rate = 1.0 mL/min; UV detection at λ = 270 nm; retention time = 15.0 min (*R* enantiomer), 20.2 min (*S* enantiomer); the absolute configuration of major enantiomer: *S*.

1-(4-Chlorophenyl)-1-propanol (2b)

^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.90 (t, 3H, J = 6.6 Hz), 1.62-1.80 (m, 2H), 1.90 (bs, 1H), 4.59 (t, 1H, J = 6.6 Hz), 7.25-7.33 (m, 4H); Chiralcel OJ column with hexane/2-propanol (97:3) as eluent; flow rate = 1.0 mL/min; UV detection at λ = 254 nm; retention time = 12.0 min (*S* enantiomer), 13.2 min (*R* enantiomer); the absolute configuration of major enantiomer: *S*.

1-(3-Tolyl)-1-propanol (2c)

^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.92 (t, 3H, J = 7.4 Hz), 1.67-1.89 (m, 3H), 2.37 (s, 3H), 4.55 (t, 1H, J = 6.6 Hz), 7.08-7.26 (m, 4H); Chiralcel OD column with hexane/2-propanol (98.5:1.5) as eluent; flow rate = 1.0 mL/min; UV detection at λ = 270 nm; retention time = 12.0 min (*R* enantiomer), 17.0 min (*S* enantiomer); the absolute configuration of major enantiomer: *S*.

1-(4-Anisyl)-1-propanol (2d)

^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.90 (t, 3H, J = 7.8 Hz), 1.60-1.84 (m, 2H), 2.17 (s, 1H), 3.81 (s, 1H), 4.55 (t, 1H, J = 7.8 Hz), 6.88 (dd, 2H, J = 2.1, 6.6 Hz), 7.26 (dd, 2H, J = 2.1, 6.6 Hz); Chiralcel OD column with hexane/2-propanol (98.5:1.5) as eluent; flow rate = 1.0 mL/min; UV detection at λ = 270 nm; retention time = 22.9 min (*R* enantiomer), 25.5 min (*S* enantiomer); the absolute configuration of major enantiomer: *S*.

***trans*-1-Phenyl-1-penten-3-ol (2e)**

^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.97 (t, 3H, J = 7.5 Hz), 1.60-1.72 (m, 3H), 4.18-4.26 (m, 1H), 6.22 (dd, 1H, J = 6.9, 15.9 Hz), 6.53 (d, 1H, J = 15.6 Hz), 7.00-7.41 (m, 5H); Chiralcel OD column with hexane/2-propanol (95:5) as eluent; flow rate = 0.8 mL/min; UV detection at λ = 270 nm; retention time = 14.4 min (*R* enantiomer), 21.9 min (*S* enantiomer); the absolute configuration of major enantiomer: *S*.

1-(2-Anisyl)-1-propanol (2f)

^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.95 (t, 3H, J = 7.5 Hz), 1.65 (s, 1H), 1.77-1.84 (m, 2H), 3.85 (s, 3H), 4.78 (t, 1H, J = 7.5 Hz), 6.87-6.98 (m, 2H), 7.22-7.31 (m, 2H); Chiralcel OD-H column with hexane/2-propanol (97:3) as eluent; flow rate = 0.5 mL/min; UV detection at λ = 254 nm; retention time = 22.6 min (*S* enantiomer), 24.8 min (*R* enantiomer); the absolute configuration of major enantiomer: *S*.

Ferrocenyl-1-propanol (2g)

^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.95 (t, 3H, J = 7.4 Hz), 1.62-1.75 (m, 2H), 1.97 (s, 1H), 4.09-4.26 (m, 10H); Chiralcel OD column with hexane/2-propanol (97:3) as eluent:; flow rate = 0.45 mL/min; UV detection at λ = 254 nm; retention time = 22.1 min (*R* enantiomer), 23.2 min (*S* enantiomer); the absolute configuration of major enantiomer: *S*.

1-(4-*N, N*-Dimethylaminophenyl)-1-propanol (2h)

^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.90 (t, 3H, J = 7.4 Hz), 1.67-1.86 (m, 3H), 2.95 (s, 6H), 4.50 (t, 1H, J = 6.7 Hz), 6.73-(dd, 2H, J = 1.8, 6.6Hz), 7.23 (dd, 2H, J = 1.9, 6.7 Hz); Chiralcel OD column with hexane/2-propanol (95:5) as eluent; flow rate = 1.0 mL/min; UV detection at λ = 240 nm; retention time for the two enantiomers: 12.4 min, 14.8 min; the absolute configuration of product was not determined.

1-(α-Naphthyl)-1-propanol (2i)

^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.04 (t, 3H, J = 7.5 Hz), 1.55 (bs, 1H), 1.88-2.10 (m, 2H), 5.40 (t, 1H, J = 7.5 Hz), 7.46-7.54 (m, 3H), 7.65 (d, 1H, J = 7.2 Hz), 7.77 (d, 1H, J = 7.8 Hz), 7.85-7.88 (m, 1H), 8.12 (d, 1H, J = 7.2 Hz); Chiralcel OD-H column with hexane/2-propanol (95:5) as eluent; flow rate = 1.0 mL/min; UV detection at λ = 254nm; retention time = 11.2 min (*S* enantiomer), 20.8 min (*R* enantiomer); the absolute configuration of major enantiomer: *S*.

1-(4-Tolyl)-1-propanol (2j)

^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.92 (t, 3H, J = 7.5 Hz), 1.74-1.84 (m, 3H), 2.36 (s, 3H), 4.57 (t, 1H, J = 7.5 Hz), 7.17 (d, 2H, J = 8.0 Hz), 7.25 (d, 2H, J = 8.1 Hz); Chiralcel OB-H column with hexane/2-propanol (98:2) as eluent; flow rate = 0.8 mL/min; UV detection at λ = 240 nm; retention time = 12.3 min (*S* enantiomer), 15.6 min (*R* enantiomer); the absolute configuration of major enantiomer: *S*.

1-(3-Anisyl)-1-propanol (2k)

^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.92 (t, 3H, J = 7.8 Hz), 1.65-1.82 (m, 3H), 3.82 (s, 3H), 4.58 (t, 1H, J = 7.8 Hz), 6.80-6.82 (m, 1H), 6.91-6.93 (m, 2H), 7.26 (t, 1H, J = 7.8 Hz); Chiralcel OB-H column with hexane/2-propanol (98:2) as eluent; flow rate = 0.8 mL/min; UV detection at λ = 240 nm;

retention time for the two enantiomers: 20.0 min, 24.9 min; the absolute configuration of product was not determined.

1-(4-Bromophenyl)-1-propanol (2*l*)

^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.91 (t, 3H, J = 7.4 Hz), 1.62-1.84 (m, 2H), 1.84-1.90 (bs, 1H), 4.56 (t, 1H, J = 7.4 Hz), 7.25 (d, 2H, J = 7.0 Hz), 7.46 (d, 2H, J = 7.0 Hz); Chiralcel OB-H column with hexane/2-propanol (98:2) as eluent; flow rate = 0.7 mL/min; UV detection at λ = 254 nm; retention time = 14.4 min (*S* enantiomer), 16.1 min (*R* enantiomer); the absolute configuration of major enantiomer: *S*.

***trans*-4-Hexen-3-ol (2m)**

^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.90 (t, 3H, J = 7.3 Hz), 1.48-1.62 (m, 2H), 1.72 (d, 3H, J = 8.1 Hz), 1.80-1.92 (bs, 1H), 3.98 (m, 1H), 5.45-5.50 (m, 1H), 5.62-5.74 (m, 1H); The enantiomeric excess of 4-hexen-3-ol was determined by GC analysis on B-PH capillary column; injection temperature 220 ^oC; detector temperature 230^oC; N_2 3.0 psi; retention time for the two enantiomers: 23.2 min, 23.6 min; the absolute configuration of product was not determined.

General Procedure for the Kinetic Experiments

The typical experiment was exemplified in the system catalyzed by racemic **DB1** and chiral **AA13.** To a dry and argon-filled 20-mL Schlenk tube were added racemic **DB1** (9.3 mg, 0.050 mmol), **AA13** (6.3 mg, 0.025 mmol) and dry CH_2Cl_2 (0.3 mL). Diethylzinc (1.0 mL, 1.0 M solution in n-hexane) was added at room temperature. After the reaction mixture was stirred for 30 min, it was cooled to 0^oC with an ice bath and benzaldehyde (53 mg, 0.50 mmol) was added in one portion. The reaction mixture was kept at 0^oC for 5 min before it was quenched with saturated ammonium chloride solution (1.0 mL). Internal standard 1-phenyl-1-ethanol (33.0 mg, 0.27 mmol) was added and then the mixture was extracted with diethyl ether (3×10 mL). The organic layers were combined, washed with brine (10 mL), dried ($MgSO_4$), filtered and concentrated to afford a colorless oil. The crude product was submitted to HPLC analysis to determine the yield of 1-phenyl-1-propanol. The conditions of HPLC were: column, Bondasphere 5μC18; flow rate, 0.6 mL/min; eluent, MeOH/H_2O (30:70); detection, 254-nm light; t_R of benzyl alcohol, 11.6 min (factor 0.8019); t_R of benzaldehyde, 17.9 min (factor 0.0153); t_R of 1-phenyl-1-

ethanol, 21.4 min (factor 1.0000); t_R of 1-phenyl-1-propanol, 50.0 min (factor 1.0140).

To determine the enantiomeric excesses of 1-phenyl-1-propanol, parallel experiments under the same reaction conditions were conducted but were quenched after stirring for 24 h at 0°C.

The Nonlinear Effect in the System of (*R*-DB1) or (*S*-DB1) and (AA13).

The experiments were performed parallelly in 1.5-mL polypropene tubes in which the concentrations of the mixed amino alcohols, diethylzinc and benzaldehyde were adjusted to 19 mM, 769 mM and 385 mM. A typical experiment was exemplified in the system catalyzed by *S*-**DB1**/**AA13** (50:50). To a 1.5-mL polypropylene microtube were added **DB1** (75 L, 83 mM in CH_2Cl_2), **AA13** (75 μL, 83 mM in CH_2Cl_2), and diethylzinc (0.5 mL, 1.0 M in n-hexane) respectively and the mixture was kept standing for 30 min at room temperature. Before benzylaldehyde (26.5 mg, 0.25 mmol) was added, the microtube was set up in the block apparatus to keep the temperature at 0°C for 30 min. After standing for 24 h at 0°C, the reaction mixture was carefully quenched with saturated ammonium chloride solution, extracted with 1 mL n-hexane and the extracts were submitted to HPLC analysis on Chiralcel OD column. The results were summarized in Table 5.

Table 5. The Enantioselectivity of the Reaction of Benzaldehyde with Diethylzinc Catalyzed by Mixing (**AA13**) with (*R*-**DB1**) or (*S*-**DB1**).

R-**DB1**: **AA13**	*ee%*	*S*-**DB1**: **AA13**	*ee%*
100:0	+91.5	100:0	-91.4
90:10	+88.8	90:10	-89.8
80:20	+86.9	80:20	-89.0
70:30	+85.1	70:30	-87.4
60:40	+82.4	60:40	-86.1
50:50	+65.9	50:50	-84.7
40:60	+49.5	40:60	-80.1
30:70	+40.5	30:70	-73.5
20:80	+22.8	20:80	-61.7
10:90	+15.6	10:90	-38.9
0:100	+15.6	0:100	+15.6

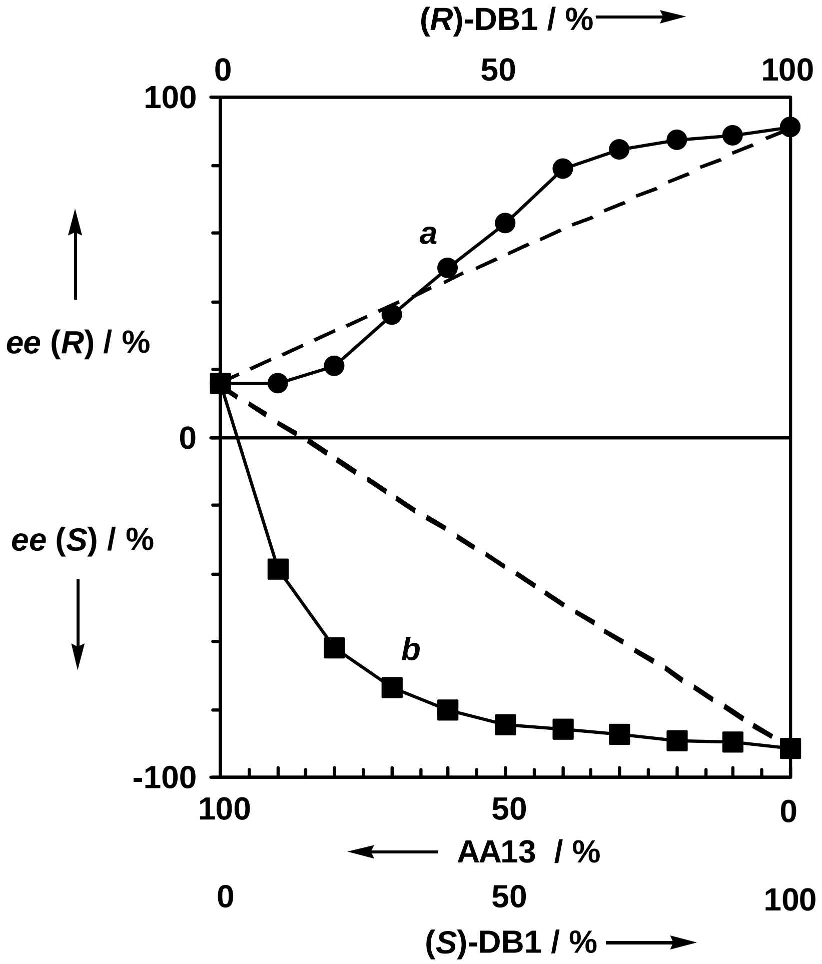


Figure 1. Enantioselectivity of the reaction of **1a** with diethylzinc catalyzed by mixing **AA13** with (*R*)-**DB1** (*a*) and (*S*)-**DB1** (*b*). The broken lines indicate the expected values when the reactivity difference between **AA13** and (*R*)-**DB1** or (*S*)-**DB1** were not considered.

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