

Supporting Information for:

Small Amounts of Achiral β -Amino Alcohols Reverse the Enantioselectivity of Chiral Catalysts in Cooperative Asymmetric Autocatalysis

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All solvents were distilled before use. Achiral catalysts **6a-f** are commercially available and were distilled under reduced pressure before use. Chiral catalysts **3**, **4**, **5** were prepared from the corresponding free amine and their spectral data were conform to the literature. Aldehyde **1** was synthesized according to a reported procedure.

Typical experimental procedures in toluene (Figure 1) :

Asymmetric Autocatalysis Initiated by 6 mol% of (1*R*,2*S*)-*N,N*-dimethylnorephedrine (DMNE **3**) and 14 mol% of achiral *N,N*-dibutylaminoethanol (DBAE **6d**): To a mixture of *chiral* (1*R*,2*S*)-DMNE **3** (3.0 mL of a 10 mM toluene solution, 0.030 mmol) and *achiral* DBAE **6d** (7.0 mL of a 10 mM toluene solution, 0.070 mmol) in toluene (2 mL) was slowly added diisopropylzinc (1.0 mL, 1 M in toluene, 1.0 mmol) at 0 °C. After stirring the mixture for 30 min, a toluene solution (3 mL) of 2-tert-butylethynylpyrimidine-5-carbaldehyde **1** (94 mg, 0.50 mmol) was added drop to drop. After 12 h at 0 °C, an aliquot (1 mL) was transferred to another flask and diluted with toluene (1.5 mL). To this second flask, diisopropylzinc (0.25 mL, 1 M in toluene, 0.25 mmol) and a toluene solution (1.5 mL) of **1** (23 mg, 0.12 mmol) were slowly added at 0

°C. After 1 h at 0 °C, additional toluene (8 mL), diisopropylzinc (1.0 mL, 1 M in toluene, 1.0 mmol) and a toluene solution (3 mL) of **1** (94 mg, 0.50 mmol) were slowly added. After 3 h at 0 °C, the reaction was quenched with a mixture of aqueous ammonia and saturated aqueous ammonium chloride solution (7 mL) and extracted by dichloromethane. The combined organic layers were dried with anhydrous sodium sulfate and evaporated under reduced pressure. Purification of the residue by silica gel TLC (developing solvent : hexane/AcOEt = 60/40) afforded 146 mg (96%) of (*R*)-2-methyl-1-[2-(3,3-dimethylbut-1-ynyl)pyrimidin-5-yl]propan-1-ol **2** with 92.2% ee (determined by HPLC using a chiral column Chiralcel OD-H, eluent : hexane:*i*-PrOH = 95:5, 1 mL/min).

Reversal of Enantioselectivity in Asymmetric Autocatalysis Initiated by 5 mol% of (1*R*,2*S*)-DMNE **3** and 15 mol% of *achiral* DBAE **6d**: To a mixture of (1*R*,2*S*)-DMNE **3** (2.5 mL of a 10 mM toluene solution, 0.025 mmol) and *achiral* DBAE **6d** (7.5 mL of a 10 mM toluene solution, 0.075 mmol) in toluene (2 mL) was slowly added diisopropylzinc (1.0 mL, 1 M in toluene, 1.0 mmol) at 0 °C. After stirring the mixture for 30 min, a toluene solution (3 mL) of pyrimidinecarbaldehyde **1** (94 mg, 0.50 mmol) was added drop to drop. After 12 h at 0 °C, an aliquot (1 mL) was transferred to another flask and diluted with toluene (1.5 mL). To this second flask, diisopropylzinc (0.25 mL, 1 M in toluene, 0.25 mmol) and a toluene solution (1.5 mL) of **1** (23 mg, 0.12 mmol) were slowly added at 0 °C. After 1 h at 0 °C, additional toluene (8 mL), diisopropylzinc (1.0 mL, 1 M in toluene, 1.0 mmol) and a toluene solution (3 mL) of **1** (94 mg, 0.50 mmol) were slowly added. After 3 h at 0 °C, the reaction was quenched with a mixture of aqueous ammonia and saturated aqueous ammonium chloride solution (7 mL) and

extracted by dichloromethane. The combined organic layers were dried with anhydrous sodium sulfate and evaporated under reduced pressure. Purification of the residue by silica gel TLC (developing solvent : hexane/AcOEt = 60/40) afforded 145 mg (95%) of (*S*)-pyrimidyl alkanol **2** with 94.3% ee (determined by HPLC using a chiral column Chiralcel OD-H, eluent : hexane:*i*-PrOH = 95:5, 1 mL/min).

Typical experimental procedures in hexane (Figure 2):

Asymmetric Autocatalysis Initiated by 16 mol% of (1*S*,2*R*)-DMNE **3** and 4 mol% of *achiral* DBAE **6d**: To a mixture of (1*S*,2*R*)-DMNE **3** (8.0 mL of a 10 mM hexane solution, 0.080 mmol) and *achiral* DBAE **6d** (2.0 mL of a 10 mM hexane solution, 0.020 mmol) in hexane (5 mL) was slowly added diisopropylzinc (1.0 mL, 1 M in hexane, 1.0 mmol) at 0 °C. After stirring the mixture for 30 min, pyrimidinecarbaldehyde **1** (94 mg, 0.50 mmol) was slowly added as a solid. After 12 h at 0 °C, an aliquot (1 mL) was transferred to another flask and diluted with toluene (1.5 mL). To this second flask, diisopropylzinc (0.25 mL, 1 M in toluene, 0.25 mmol) and a toluene solution (1.5 mL) of **1** (23 mg, 0.12 mmol) were slowly added at 0 °C. After 1 h at 0 °C, additional toluene (8 mL), diisopropylzinc (1.0 mL, 1 M in toluene, 1.0 mmol) and a toluene solution (3 mL) of **1** (94 mg, 0.50 mmol) were slowly added. After 3 h at 0 °C, the reaction was quenched with a mixture of aqueous ammonia and saturated aqueous ammonium chloride solution (7 mL) and extracted by dichloromethane. The combined organic layers were dried with anhydrous sodium sulfate and evaporated under reduced pressure. Purification of the residue by silica gel TLC (developing solvent : hexane/AcOEt = 60/40) afforded 142 mg (93%) of (*S*)-pyrimidyl alkanol **2**

with 95.9% ee (determined by HPLC using a chiral column Chiralcel OD-H, eluent : hexane:*i*-PrOH = 95:5, 1 mL/min).

Reversal of Enantioselectivity in Asymmetric Autocatalysis Initiated by 15 mol% of (1*S*,2*R*)-DMNE **3** and 5 mol% of achiral DBAE **6d**: To a mixture of (1*S*,2*R*)-DMNE **3** (7.5 mL of a 10 mM hexane solution, 0.075 mmol) and achiral DBAE **6d** (2.5 mL of a 10 mM hexane solution, 0.025 mmol) in hexane (5 mL) was slowly added diisopropylzinc (1.0 mL, 1 M in hexane, 1.0 mmol) at 0 °C. After stirring the mixture for 30 min, pyrimidinecarbaldehyde **1** (94 mg, 0.50 mmol) was slowly added as a solid. After 12 h at 0 °C, an aliquot (1 mL) was transferred to another flask and diluted with toluene (1.5 mL). To this second flask, diisopropylzinc (0.25 mL, 1 M in toluene, 0.25 mmol) and a toluene solution (1.5 mL) of **1** (23 mg, 0.12 mmol) were slowly added at 0 °C. After 1 h at 0 °C, additional toluene (8 mL), diisopropylzinc (1.0 mL, 1 M in toluene, 1.0 mmol) and a toluene solution (3 mL) of **1** (94 mg, 0.50 mmol) were slowly added. After 3 h at 0 °C, the reaction was quenched with a mixture of aqueous ammonia and saturated aqueous ammonium chloride solution (7 mL) and extracted by dichloromethane. The combined organic layers were dried with anhydrous sodium sulfate and evaporated under reduced pressure. Purification of the residue by silica gel TLC (developing solvent : hexane/AcOEt = 60/40) afforded 140 mg (92%) of (*R*)-pyrimidyl alkanol **2** with 98.3% ee (determined by HPLC using a chiral column Chiralcel OD-H, eluent : hexane:*i*-PrOH = 95:5, 1 mL/min).

Amplification of enantiomeric excesses of alkanol **2 at the two stages in asymmetric autocatalysis initiated by a mixture of chiral DMNE and achiral DBAE of various ratios in hexane.**

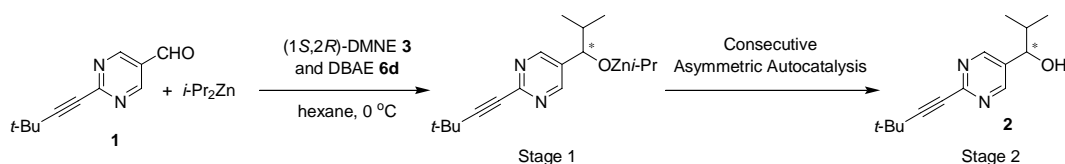


Table S-1. Asymmetric autocatalysis initiated by a mixture of chiral DMNE and achiral DBAE of various ratios in hexane.

entry	catalysts		product				
	(1 <i>S</i> ,2 <i>R</i>)-DMNE (mol%)	DBAE (mol%)	stage 1		stage 2		
			ee (%)	config	yield (%)	ee (%)	config.
1	20	0	92.8	<i>S</i>	98	98.8	<i>S</i>
2	18	2	94.3	<i>S</i>	95	98.8	<i>S</i>
3	16	4	38.5	<i>S</i>	93	95.9	<i>S</i>
4	15	5	80.9	<i>R</i>	92	98.3	<i>R</i>
5	14	6	84.7	<i>R</i>	93	98.5	<i>R</i>
6	12	8	88.9	<i>R</i>	92	98.3	<i>R</i>
7	10	10	89.5	<i>R</i>	97	98.7	<i>R</i>
8	6	14	66.6	<i>R</i>	93	96.5	<i>R</i>
9	2	18	29.6	<i>R</i>	92	95.5	<i>R</i>

Typical experimental procedure of the kinetic studies: To a mixture of (1*R*,2*S*)-DMNE **3** (5.0 mL of a 10 mM toluene solution, 0.050 mmol) and *achiral* DBAE **6d** (5.0 mL of a 10 mM toluene solution, 0.050 mmol) and naphthalene (0.26 g, 0.50 mmol,

internal standard) in toluene (2 mL) was slowly added diisopropylzinc (1.0 mL, 1 M in toluene, 1.0 mmol) at 0 °C. After stirring the mixture for 30 min, a toluene solution (3 mL) of pyrimidinecarbaldehyde **1** (94 mg, 0.50 mmol) was rapidly added. Aliquots (0.5 mL) were regularly (every 30 s) taken *via* syringes and quenched with a mixture of aqueous ammonia and saturated aqueous ammonium chloride solution (2 mL). The organic layers were filtered and the amounts of product **2** were measured by HPLC (column Sumipax ODS A-05-601, eluent : MeOH:H₂O = 70:30, 0.8 mL/min) by using naphthalene as internal standard.