

**CATALYTIC ASYMMETRIC SYNTHESIS AND ASYMMETRIC
AUTOCATALYSIS OF CHIRAL 5,5'-(3,3'-BIPYRIDYL)-
DIALKANEDIOL**

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Abstract – (*S,S*)-(-)-5,5'-(3,3'-Bipyridyl)dialkanediols (**5a**, **b**) with up to 98.6% e.e. was synthesized by the enantioselective addition of dialkylzincs to 3,3'-bipyridine-5,5'-dicarbaldehyde (**4**) using *N,N*-dipropylnorephedrine as a chiral catalyst. Chiral diol (**5a**) was found to work as an asymmetric autocatalyst in the enantioselective addition of diisopropylzinc to aldehyde (**4**).

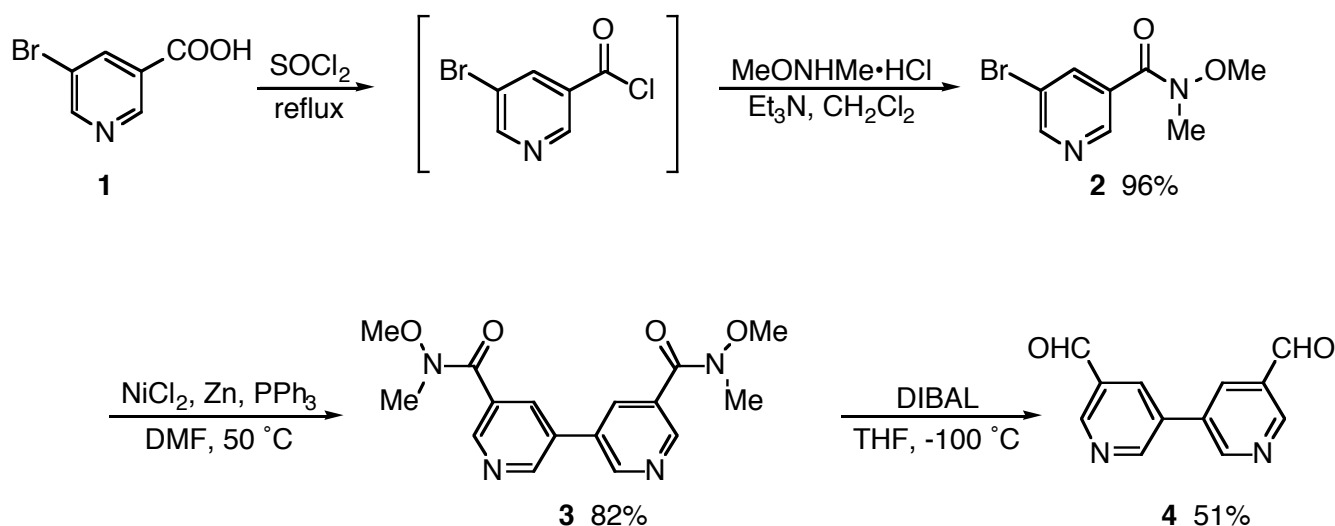
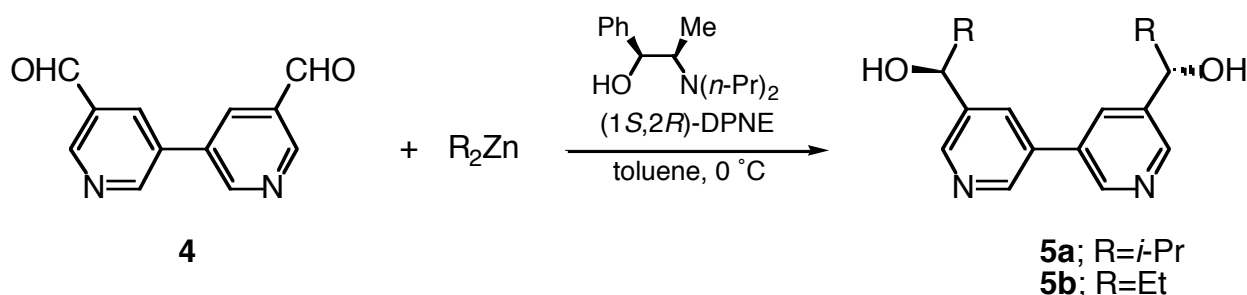
Chiral diols with C_2 -symmetry axis are known to be useful ligands in asymmetric synthesis.^{1,2} However, the synthesis of chiral diols by the enantioselective alkylation of dialdehyde has not been extensively examined.³ On the other hand, asymmetric autocatalysis,⁴ in which a chiral product catalyzes its own production, has attracted much attention. An asymmetric autocatalysis of a chiral diol is important because a bifunctional molecule automultiplies by constructing two stereogenic centers.⁵ We previously reported asymmetric autocatalysis of chiral pyridyl alkanols⁶ in the enantioselective alkylation of pyridine-3-carbaldehyde and its derivatives with dialkylzinc.

In this paper, we report an enantioselective dialkylation of 3,3'-bipyridine-5,5'-dicarbaldehyde (**4**) with dialkylzincs which affords highly enantiomerically enriched (*S,S*)-5,5'-(3,3'-bipyridyl)dialkanediols (**5a**, **b**). We also report an asymmetric autocatalytic reaction of (*S,S*)-(-)-5,5'-bis(1-hydroxy-2-methylpropyl)-3,3'-bipyridine (**5a**), in which a chiral diol (**5a**) automultiplies without the need for any other chiral auxiliary, in the enantioselective dialkylation of dicarbaldehyde (**4**) with diisopropylzinc (*i*-Pr₂Zn).

Synthetic route of 3,3'-bipyridine-5,5'-dicarbaldehyde (**4**) is shown in Scheme 1. 5-Bromonicotinic acid (**1**) was converted into acid chloride using thionyl chloride. Subsequent treatment with *N,O*-dimethylhydroxylamine hydrochloride and triethylamine gave Weinreb's amide (**2**)⁷ in a total yield of 96% from acid (**1**). Nickel(0)-mediated homocoupling⁸ of **2** afforded 3,3'-bipyridine (**3**) in 82%. Subsequent reduction of **3** using DIBAL in THF at -100 °C gave dialdehyde (**4**) in 51%.

The results of the catalytic enantioselective dialkylation of dialdehyde (**4**) are summarized in Table 1. When dialdehyde (**4**) was treated with *i*-Pr₂Zn in the presence of (1*S*,2*R*)-*N,N*-dipropylnorephedrine (DPNE),⁹ enantiomerically enriched diol ((*S,S*)-(-)-**5a**)¹⁰ with 83.6% e.e. (*dllmeso* = 68/32) was obtained (Entry 1). When the amount of (1*S*,2*R*)-DPNE was increased, the reaction afforded almost enantiomerically pure

Scheme 1.

Table 1. Enantioselective synthesis of chiral (*S,S*)-(-)-5,5'-(3,3'-bipyridyl)dialkanediols (**5a**, **b**) using (1*S*,2*R*)-DPNE

Entry	R	Chiral diol (2)		
		Yield (%)	E.e.(%) ^a	<i>dl</i> / <i>meso</i> ^a
1 ^b	<i>i</i> -Pr	5a 34	83.6	68 / 32
2 ^c	<i>i</i> -Pr	5a 52	98.6	85 / 15
3 ^c	Et	5b 47	92.3	72 / 28

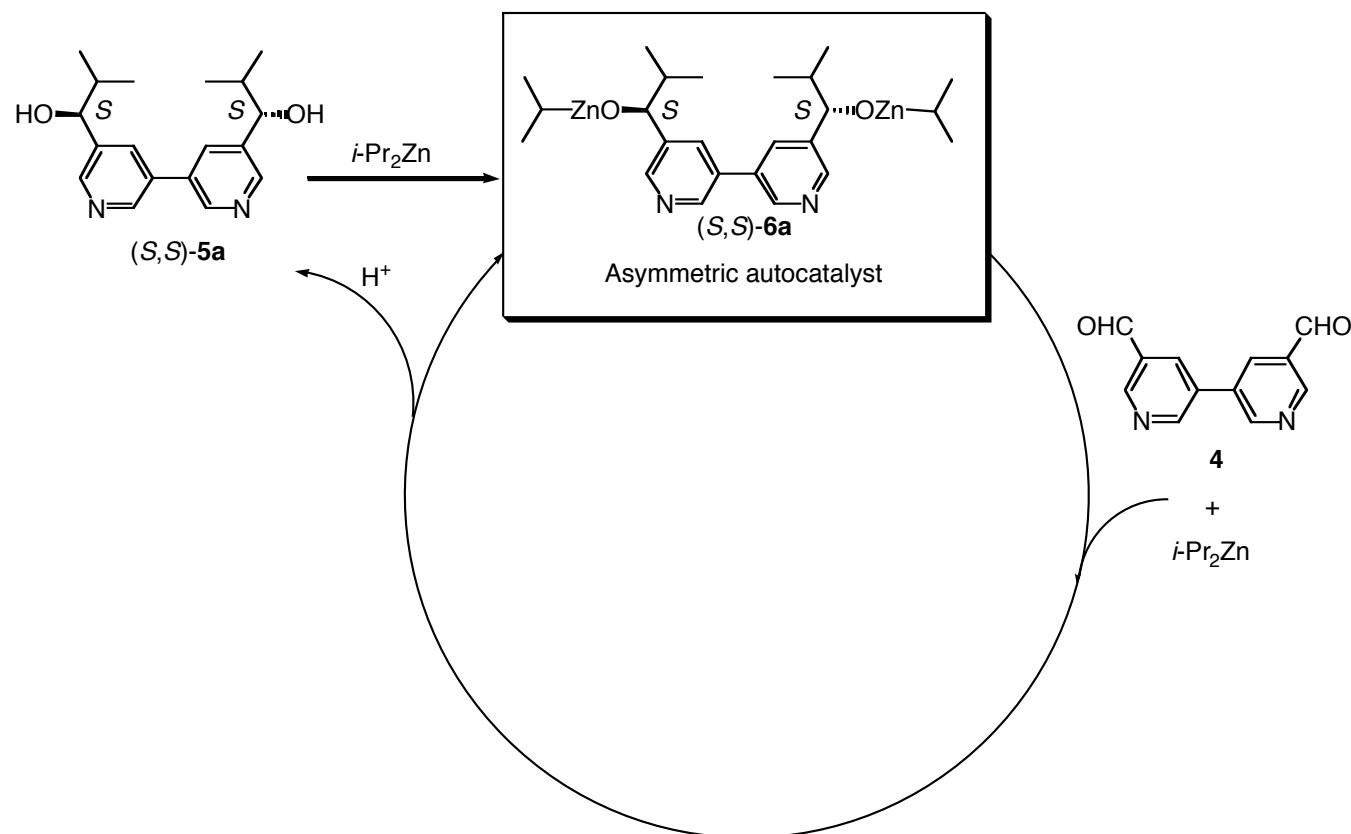
^a Determined by HPLC analyses using a chiral column (Chiralpak AD). ^b Molar ratio. (1*S*,2*R*)-DPNE : **4** : *i*-Pr₂Zn = 0.4 : 1.0 : 10. ^c Molar ratio. (1*S*,2*R*)-DPNE : **4** : *i*-Pr₂Zn = 0.8 : 1.0 : 10.

(*S,S*)-**5a** (98.6% e.e.) in a yield of 52% (*dl/meso* = 85/15) (Entry 2). In a similar manner, enantioselective diethylation of (**4**) using diethylzinc in the presence of (1*S*,2*R*)-DPNE afforded (*S,S*)-(-)-**5b**¹⁰ with a high enantiomeric purity (92.3% e.e., *dl/meso* = 72/28) (Entry 3).

Next, the enantioselective addition of *i*-Pr₂Zn to dialdehyde (**4**) was examined by using chiral (*S,S*)-**5a** as an asymmetric autocatalyst. The results are shown in Table 2. The product ((*S,S*)-**5a**), possessing the same structure and the same configuration as those of the initial autocatalyst ((*S,S*)-**5a**) (>99.5% e.e., 10

mol%),¹¹ was newly formed with 18.8% e.e. (Entry 1). When the asymmetric autocatalyst with 98.6% e.e. was used (40 mol%), improved enantioselectivity of 28.9% e.e. was observed (Entry 3). We suppose that chiral bis(alkylzinc alkoxide) ((*S,S*)-**6a**) formed *in situ* by the treatment of diisopropylzinc with (*S,S*)-**5a** acts as an asymmetric autocatalyst for its own production.

Table 2. Asymmetric autocatalytic reaction of chiral (*S,S*)-5,5'-(3,3'-bipyridyl)dialkanediol (**5a**)



Entry	Asymmetric autocatalyst (5a)		Asymmetric autocat. & newly formed 5a		Newly formed diol (5a) ^a		
	E.e./ % ^b	<i>dl</i> / <i>meso</i> ^b	E.e./ % ^b	Yield/ %	E.e./ %	<i>dl</i> / <i>meso</i>	
1 ^c	5a >99.5	>99.5 / <0.5	46.6	5a 34	18.8	56 / 44	
2 ^d	5a 78.2	65 / 35	48.9	5a 21	14.1	53 / 47	
3 ^e	5a 98.6	85 / 15	75.4	5a 29	28.9	58 / 42	

^a The amounts of the (*S,S*)- and (*R,R*)- enantiomers and *meso*- isomer of the diol used as an initial asymmetric autocatalyst were subtracted from that of the obtained diol by calculation. ^b Determined by HPLC analyses using a chiral column (Chiralpak AD). ^c Molar ratio. (*S,S*)-**5a** : **4** : *i*-Pr₂Zn = 0.1 : 1.0 : 10. ^d Molar ratio. (*S,S*)-**5a** : **4** : *i*-Pr₂Zn = 0.2 : 1.0 : 10. ^e Molar ratio. (*S,S*)-**5a** : **4** : *i*-Pr₂Zn = 0.4 : 1.0 : 10.

In summary, highly enantiomerically enriched (*S,S*)-5,5'-(3,3'-bipyridyl)dialkanediols (**5a**, **b**) with up to 98.6% e.e. were synthesized by the enantioselective addition of dialkylzincs to 3,3'-bipyridine-5,5'-dicarbaldehyde (**4**) using (1*S*,2*R*)-*N,N*-dipropylnorephedrine (DPNE) as a chiral catalyst. Furthermore, chiral diol ((*S,S*)-**5a**) automultiplied in the asymmetric autocatalytic reaction of dialdehyde (**4**) with diisopropylzinc.¹²

EXPERIMENTAL

General. Optical rotations were measured with Jasco DIP-1000 polarimeter. IR spectra were recorded with Horiba FT-210 spectrophotometer. ¹H and ¹³C NMR spectra were measured with Bruker DPX300 spectrometer using tetramethylsilane as an internal standard. High resolution mass spectra (HRMS) were obtained with Hitachi M-80B mass spectrometer. Toluene was distilled from calcium hydride and dried over molecular sieves 4A. All reactions were carried out under an argon atmosphere.

3-Bromo-5-(*N*-methoxy-*N*-methylcarbamoyl)pyridine (2). Thionyl chloride (30 mL, 411 mmol) was added to 5-bromonicotinic acid (**1**) (2.02 g, 10.0 mmol) and the mixture was refluxed for 6 h. Excess of thionyl chloride was removed by distillation, and then the resulted mixture was evaporated to dryness under reduced pressure. The residue (acid chloride) was dissolved in dichloromethane (20 mL), then triethylamine (2.8 mL, 20 mmol) and *N,O*-dimethylhydroxylamine hydrochloride (975 mg, 10.0 mmol) were added successively at 0 °C. The mixture was warmed to rt and stirred for 24 h. The reaction was quenched by the addition of sat. aq. sodium bicarbonate (20 mL). The reaction mixture was extracted twice with 20 mL of ethyl acetate. The combined organic layer was dried over anhydrous sodium sulfate and evaporated to dryness under reduced pressure. Purification of the residue by flash column chromatography on silica gel (hexane : acetone = 7 : 1) afforded Weinreb's amide (**2**) as a colorless oil. 2.35 g. Yield 96%. IR (neat) ν/cm^{-1} = 1647; ¹H NMR (300 MHz, CDCl₃) δ 3.39 (s, 3H), 3.58 (s, 3H), 8.18 (dd, *J* = 2.0, 2.0 Hz, 1H), 8.75 (d, *J* = 2.0 Hz, 1H), 8.88 (d, *J* = 2.0 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 33.0, 61.3, 120.1, 130.9, 138.5, 147.2, 152.3, 165.6; HRMS found *m/z* 243.9843, calcd for C₈H₉N₂O₂Br: 243.9848.

5,5'-Bis(*N*-methoxy-*N*-methylcarbamoyl)-3,3'-bipyridine (3). A suspension of NiCl₂ (560 mg, 4.4 mmol), zinc powder (288 mg, 4.4 mmol) and triphenylphosphine (4.63 g, 17.6 mmol) in DMF (15mL) was heated at 50 °C for 1 h, and amide (**2**) (2.16 g, 8.8 mmol) in DMF (5 mL) was added. After the reaction mixture was stirred for 5 h at 50 °C, the mixture was cooled to rt and poured into 30 mL of 5% aqueous NH₃. The resulted mixture was filtered and the filtrate was extracted with ethyl acetate. The combined organic layer was dried over anhydrous sodium sulfate and evaporated to dryness under reduced pressure. Purification of the residue by flash column chromatography on silica gel (hexane : CH₂Cl₂ : acetone : MeOH = 12 : 8 : 3 : 1) afforded 3,3'-bipyridine (**3**). 979 mg. Yield 81.5%. Colorless powder (recrystallized from hexane – ethyl acetate). mp 87.0 – 88.0 °C; IR (KBr) ν/cm^{-1} = 1643; ¹H NMR (300 MHz, CDCl₃) δ 3.44 (s, 6H), 3.61 (s, 6H), 8.27 (dd, *J* = 2.1, 2.1 Hz, 2H), 8.95 (d, *J* = 2.1 Hz, 2H), 9.02 (d, *J* = 2.1 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 33.2, 61.4, 130.1, 132.2, 134.7, 148.9, 149.5, 166.8; HRMS found *m/z* 330.1316, calcd for C₁₆H₁₈N₄O₄: 330.1329; Anal. Calcd for C₁₆H₁₈N₄O₄: C, 58.17; H, 5.49; N, 16.96. Found: C, 58.50; H, 5.71; N, 16.84.

3,3'-Bipyridine-5,5'-dicarbaldehyde (4). A toluene solution of 1.0 M DIBAL (10 mL, 10.0 mmol) was added dropwise to a solution of 3,3'-bipyridine (**3**) (826 mg, 2.5 mmol) in THF (15 mL) at $-100\text{ }^{\circ}\text{C}$, and the mixture was stirred for 1 h. The reaction was quenched by the addition of 15 mL of mixed solvent [THF : H₂O = 1 : 1 (v/v)] at $-100\text{ }^{\circ}\text{C}$, and the resulted mixture was warmed to rt. After stirring for 1 h, the mixture was filtered through Celite and the filtrate was extracted with ethyl acetate. The combined organic layer was dried over anhydrous sodium sulfate and evaporated to dryness under reduced pressure. Purification of the residue by flash column chromatography on silica gel (ethyl acetate : CHCl₃ = 1 : 1) afforded **4**. 273 mg. Yield 51%. Colorless powder (recrystallized from hexane – ethyl acetate). mp 219.0 – 220.0 $^{\circ}\text{C}$; IR (KBr) ν/cm^{-1} = 1693; ¹H NMR (300 MHz, CDCl₃) δ 8.43 (dd, J = 1.9, 2.2 Hz, 2H), 9.15 (d, J = 2.2 Hz, 2H), 9.18 (d, J = 1.9 Hz, 2H), 10.25(s, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 131.5, 132.9, 133.9, 152.1, 152.9, 190.0; HRMS found m/z 212.0592, calcd for C₁₂H₈N₂O₂: 212.0586; Anal. Calcd for C₁₂H₈N₂O₂: C, 67.92; H, 3.80; N, 13.20. Found: C, 67.87; H, 3.89; N, 13.21.

A typical experimental procedure for the enantioselective dialkylation of dialdehyde (4) using (1S,2R)-N,N-dipropylnorephedrine (DPNE) (Table 2, Entry 2). To a mixture of (1S,2R)-DPNE (56.5 mg, 0.24 mmol) and dialdehyde (**4**) (63.7 mg, 0.3 mmol) in toluene (3.0 mL), 1 M toluene solution of diisopropylzinc (3.0 mL, 3.0 mmol) was added at 0 $^{\circ}\text{C}$. After the mixture was stirred for 51 h at 0 $^{\circ}\text{C}$, the reaction was quenched by the addition of 1 M hydrochloric acid (5 mL) followed by the addition of sat. aq. sodium bicarbonate (15 mL). The resulted mixture was filtered through Celite and the filtrate was extracted with ethyl acetate. The combined organic layer was dried over anhydrous sodium sulfate and evaporated to dryness under reduced pressure. Purification of the crude residue on silica gel TLC (developing solvent. CH₂Cl₂ : MeOH = 10 : 1) gave diol (**5a**) (46.7 mg, 52%).

(S,S)-(-)-5,5'-Bis(1-hydroxy-2-methylpropyl)-3,3'-bipyridine (5a). Colorless oil. Enantiomeric excess of (S,S)-**5a** was determined to be 98.6% e.e. ($dll/meso$ = 85.3/14.7) by HPLC analysis using a chiral column (Daicel Chiralpak AD: 4 x 250 mm, 254 nm UV detector, rt, eluent: 10% 2-propanol in hexane, flow rate: 1.0 mL/min, retention time: 16.4 min for the minor isomer, 21.7 min for the *meso*- isomer and 30.1 min for the major isomer). Specific optical rotation of (S,S)-**5a** with >99.5% e.e. ($dll/meso$ = >99.5/<0.5) is shown in ref. 11. IR (neat) ν/cm^{-1} = 3228; ¹H NMR (300 MHz, CDCl₃) δ 0.85 (d, J = 6.7 Hz, 6H), 1.02 (d, J = 6.7 Hz, 6H), 2.01 (dq, J = 6.5, 6.7, 6.7 Hz, 2H), 4.50 (d, J = 6.5 Hz, 2H), 4.81 (br s, 2H), 7.79 (dd, J = 1.7, 1.7 Hz, 2H), 8.26 (d, J = 1.7 Hz, 2H), 8.40 (d, J = 1.7 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 18.0, 18.8, 35.2, 76.9, 132.5, 132.7, 140.2, 146.1, 147.7; Anal. Calcd for C₁₈H₂₄N₂O₂: C, 71.97; H, 8.05; N, 9.33. Found: C, 71.92; H, 8.10; N, 9.41.

(S,S)-(-)-5,5'-Bis(1-hydroxypropyl)-3,3'-bipyridine (5b). Colorless oil. Yield 47%. Enantiomeric excess of (S,S)-**5b** was determined to be 92.3% e.e. ($dll/meso$ = 71.8/28.2) by HPLC analysis using a chiral column (Daicel Chiralpak AD: 4 x 250 mm, 254 nm UV detector, rt, eluent: 10% 2-propanol in hexane, flow rate: 1.0 mL/min, retention time: 16.8 min for the minor isomer, 21.3 min for *meso*- isomer and 25.4 min for the major isomer). $[\alpha]_{\text{D}}^{23}$ -28.2° (c 0.5, MeOH); IR (neat) ν/cm^{-1} = 3340; ¹H NMR (300 MHz, CDCl₃) δ 0.94 (t, J = 7.3 Hz, 6H), 1.75 (dq, J = 6.4, 7.3 Hz, 4H), 4.69 (t, J = 6.4 Hz, 2H), 4.94 (br s, 2H), 7.83 (br s, 2H), 8.29 (br s, 2H), 8.41 (br s, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 10.0, 31.9, 72.8, 132.3, 133.0, 141.3, 146.0, 147.1; HRMS found m/z 272.1527, calcd for C₁₆H₂₀N₂O₂:

272.1526.

A typical experimental procedure of the asymmetric autocatalytic reaction using chiral diol (5a) (Table 2, Entry 3). To a mixture of dialdehyde (**4**) (63.7 mg, 0.3 mmol) and diol ((*S,S*)-**5a**) (36.0 mg, 0.12 mmol) with 98.6% e.e. (*dllmeso* = 85.3/14.7) [containing (*S,S*)-isomer (30.5 mg), (*R,R*)-isomer (0.2 mg) and *meso* isomer (5.3 mg)] in toluene (4.1 mL) was added *i*-Pr₂Zn (3.0 mmol, 3.0 mL of 1 M toluene solution) at 0 °C. After the reaction mixture was stirred for 44 h at 0 °C, the reaction was quenched by the addition of 1 M hydrochloric acid (5 mL). After the mixture was neutralized by the addition of sat. aq. sodium bicarbonate (15 mL), the mixture was filtered through Celite. The filtrate was extracted with ethyl acetate. The extract was dried over anhydrous sodium sulfate and evaporated under reduced pressure. Purification of the residue on silica gel TLC (developing solvent. CH₂Cl₂ : MeOH = 10 : 1) gave diol (**5a**) (62.3 mg, 0.207 mmol), which contained the newly formed diol and the initially used diol as an asymmetric autocatalyst. HPLC analysis using a chiral column (Chiralpak AD, eluent: 10% 2-propanol in hexane; flow rate: 1.0 mL/min; 254 nm UV detector) showed that the enantiomeric purity of the obtained diol ((*S,S*)-(-)-**5a**) was 75.4% e.e. (*dllmeso* = 73.7/26.3). Therefore, the obtained diol ((*S,S*)-**5a**) contained (*S,S*)-isomer (40.3 mg), (*R,R*)-isomer (5.6 mg) and *meso* isomer (16.4 mg). The amount of the newly formed diol (**5a**) was calculated as 62.3 – 36.0 = 26.3 mg (29% yield), consisting of the major (*S,S*)-enantiomer (40.3 – 30.5 = 9.8 mg), the minor (*R,R*)-enantiomer (5.6 – 0.2 = 5.4 mg) and the *meso* isomer (16.4 – 5.3 = 11.1 mg). As a result, the enantiomeric purity of the newly formed diol ((*S,S*)-**5a**) was calculated as 28.9% e.e. (*dllmeso* = 57.8/42.2).

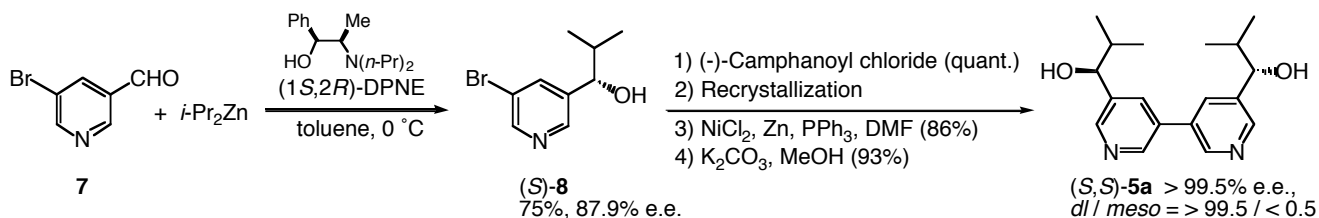
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REFERENCES AND NOTES

1. Review: J. K. Whitesell, *Chem. Rev.*, 1989, **89**, 1581.
2. (a) C. Bolm, M. Ewald, and M. Felder, *Chem. Ber.*, 1992, **125**, 1205; (b) Y. Ukaji, Y. Shimizu, Y. Kenmoku, A. Ahmed, and K. Inomata, *Chem. Lett.*, 1997, 59; (c) K. Ding, A. Ishii, and K. Mikami, *Angew. Chem., Int. Ed. Engl.*, 1999, **38**, 497; (d) D. Seebach, I. M. Lyapkalo, and R. Dahinden, *Helv. Chim. Acta*, 1999, **82**, 1829.
3. (a) K. Soai, H. Hori, and M. Kawahara, *Chem. Commun.*, 1992, 106; (b) D. Seebach, A. K. Beck, B. Schmidt, and Y. M. Wang, *Tetrahedron*, 1994, **50**, 4363.
4. (a) K. Soai, T. Shibata, H. Morioka, and K. Choji, *Nature*, 1995, **378**, 767; (b) T. Shibata, H. Morioka, T. Hayase, K. Choji, and K. Soai, *J. Am. Chem. Soc.*, 1996, **118**, 471; (c) T. Shibata, K. Choji, H. Morioka, T. Hayase, and K. Soai, *Chem. Commun.*, 1996, 751; (d) T. Shibata, S. Yonekubo, and K. Soai, *Angew. Chem., Int. Ed. Engl.*, 1999, **38**, 659.
5. (a) Asymmetric autocatalysis of a chiral diol; K. Soai, T. Hayase, C. Shimada, and K. Isobe, *Tetrahedron: Asymmetry*, 1994, **5**, 789; (b) cf. Asymmetric autoinduction of a chiral diol; K. Soai, Y. Inoue, T. Takahashi, and T. Shibata, *Tetrahedron*, 1996, **42**, 13355.

6. (a) T. Shibata, H. Morioka, S. Tanji, T. Hayase, Y. Kodaka, and K. Soai, *Tetrahedron Lett.*, 1996, **37**, 8783; (b) K. Soai, S. Niwa, and H. Hori, *Chem. Commun.*, 1990, 982.
7. S. Nahm and S. M. Weinreb, *Tetrahedron Lett.*, 1981, **22**, 3815.
8. C. Bolm, M. Ewald, M. Felder, and G. Schlingloff, *Chem. Ber.*, 1992, **125**, 1169.
9. (a) K. Soai, T. Hayase, K. Takai, and T. Sugiyama, *J. Org. Chem.*, 1994, **59**, 7908; (b) K. Soai, S. Yokoyama, and T. Hayasaka, *J. Org. Chem.*, 1991, **56**, 4264; For reviews on the enantioselective addition of dialkylzincs to aldehydes: (c) K. Soai and S. Niwa, *Chem. Rev.*, 1992, **92**, 833; (d) K. Soai and T. Hayase, *Yuki Gosei Kagaku Kyokaiishi (J. Synth. Org. Chem., Jpn.)*, 1995, **53**, 138; (e) R. Noyori and M. Kitamura, *Angew. Chem., Int. Ed. Engl.*, 1991, **30**, 49.
10. Absolute configuration is tentatively assigned based on our previous result that (1*S*,2*R*)-DPNE catalyzes the enantioselective addition of *i*-Pr₂Zn to benzaldehyde to afford (*S*)-2-methyl-1-phenyl-1-propanol (ref. 9a).
11. Diol ((*S,S*)-**5a**) with >99.5% e.e. (*dl*/*meso* = >99.5/<0.5) was synthesized as follows: Enantioselective isopropylation of 5-bromopyridine-3-carbaldehyde (**7**), derived from Weinreb's amide (**2**) by the reduction with DIBAL, using 50 mol% of (1*S*,2*R*)-DPNE as a chiral catalyst afforded (*S*)-**8** in the yield of 75% with 87.9% e.e. The e.e. of **8** was increased by recrystallization of the corresponding camphanic acid ester from petroleum ether, and nickel(0)-mediated homocoupling⁸ followed by hydrolysis gave (*S,S*)-**5a** with >99.5% e.e. ($[\alpha]_D^{21} -58.2^\circ$ (*c* 0.6, MeOH)).



(*S*)-1-{5-bromo(3-pyridyl)}-2-methyl-1-propanol (8**).** Colorless oil. Enantiomeric excess of (*S*)-**8** was determined to be 87.9% e.e. by HPLC analysis using a chiral column (Daicel Chiralcel OD-H: 4 x 250 mm, 254 nm UV detector, rt, eluent: 0.4% 2-propanol in hexane, flow rate: 1.0 mL/min, retention time: 130 min for the major isomer, 149 min for the minor isomer). $[\alpha]_D^{22} -58.6^\circ$ (*c* 10.5, CHCl₃); IR (neat) $\nu/\text{cm}^{-1} = 3278$; ¹H NMR (300 MHz, CDCl₃) δ 0.83 (d, *J* = 6.7 Hz, 3H), 0.95 (d, *J* = 6.7 Hz, 3H), 1.94 (dq, *J* = 6.2, 6.7, 6.7 Hz, 1H), 4.39 (d, *J* = 6.2 Hz, 1H), 4.51 (br s, 1H), 7.85 (dd, *J* = 2.0, 2.0 Hz, 1H), 8.27 (d, *J* = 2.0 Hz, 1H), 8.42 (d, *J* = 2.0 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 17.6, 18.6, 35.1, 76.1, 120.6, 137.1, 141.4, 145.9, 148.9; HRMS found *m/z* 229.0111, calcd for C₉H₁₂BrNO: 229.0102.

12. In the reaction of dialkylzinc and 2,2'-bipyridine-5,5'-dicarbaldehyde, unprecedented alkylation to the pyridine ring occurred. The results will be reported elsewhere.