



0957-4166(95)00142-5

A Novel Synthesis of Optically Active C_2 -Symmetric Pyridine Derivatives. Efficient Reaction of Chiral Triflates with 2-Picolylithium Reagents.

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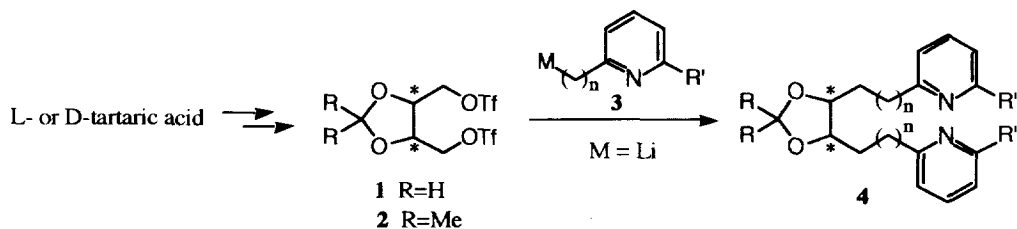
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Abstract: A variety of optically active C_2 -symmetric pyridine derivatives have been prepared from L- or D-tartaric acid as a chiral source via efficient coupling reactions of triflates with 2-picolylithium reagents, and the utility of **17** and **18** as chiral ligands in the catalytic enantioselective addition of diethylzinc to benzaldehyde has been demonstrated (up to 41% ee). The synthetic procedure for the corresponding *meso*-isomer was also described.

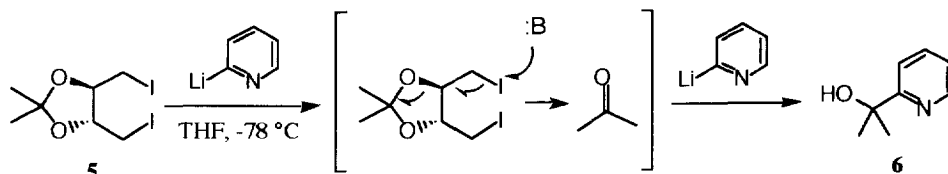
Pyridine and oligopyridine derivatives are an important class of compounds useful not only as synthetic intermediates¹ but also as chelating agents over a broad range of coordination² and supramolecular chemistry.³ Recently, chiral pyridine and oligopyridine derivatives have gained considerable attention because of their utility as efficient ligands in several asymmetric transformations.⁴ At present, however, synthetic routes to these compounds are rather limited in general applicability. Here, we wish to report a novel straightforward approach to optically active C_2 -symmetric pyridine derivatives.

Our synthetic strategy is based upon a convenient method to form carbon-carbon bonds at the carbon centers bearing β -oxygen atoms via triflate intermediates which was developed in our laboratory.⁵ As outlined in Scheme 1, we expected that the introduction of pyridine functionality onto the side chain of ditriflates **1** or **2** would provide a new entry to the construction of a variety of chiral pyridine derivatives **4** with a C_2 -symmetry axis. Since the starting chiral source, tartaric acid,⁶ is available in both L- and D-forms, the procedure might be particularly advantageous for deriving both enantiomers of **4**.



Scheme 1

To realize the above expectation we first examined the reaction with 2-pyridyllithium (**3**; R'=H, n=0). Unfortunately, triflates **1** and **2** were completely unreactive toward this reagent under a variety of conditions. The use of iodide **5** as an alternative substrate gave 2-pyridylcarbinol **6** as the only isolable product via β -elimination of the iodide (Scheme 2).



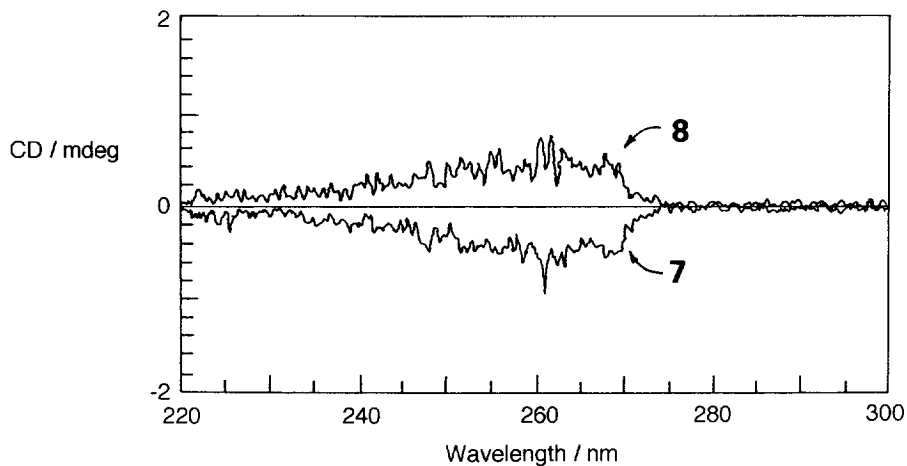
Scheme 2

On the other hand, the reaction of **1** or **2** with 2-picolylithium (**3**; R'=H, n=1), prepared by lithiation of 2-picoline with 1 eq of LDA, proceeded cleanly at $-100\text{ }^{\circ}\text{C}$ ⁹ to provide **7-10** in good yields.¹⁰ Similarly, coupling reactions with 2,6-lutidine and 6-methyl-2,2'-bipyridine¹¹ were also achieved in moderate yields (compounds **11-16**). The results including specific rotations are summarized in Table 1.

Table 1. Chiral Pyridine Derivatives Prepared from **1** and **2**.

	(R = H, R' = H; 82%) ^a (R = Me, R' = H; 80%) ^a (R = H, R' = Me; 41%) ^a	
7 : R=H, R'=H $[\alpha]_{\text{D}}^{24} -60.98$ (<i>c</i> 1.02) ^b		8 : R=H, R'=H $[\alpha]_{\text{D}}^{23} +60.63$ (<i>c</i> 1.28) ^b
9 : R=Me, R'=H $[\alpha]_{\text{D}}^{23} -43.22$ (<i>c</i> 0.472) ^b		10 : R=Me, R'=H $[\alpha]_{\text{D}}^{25} +43.16$ (<i>c</i> 0.519) ^b
11 : R=H, R'=Me $[\alpha]_{\text{D}}^{24} -53.50$ (<i>c</i> 0.40) ^b		12 : R=H, R'=Me $[\alpha]_{\text{D}}^{24} +54.10$ (<i>c</i> 0.72) ^b
	(R = H; 46%) ^a (R = Me; 43%) ^a	
13 : R=H $[\alpha]_{\text{D}}^{24} -45.7$ (<i>c</i> 1.44) ^b		14 : R=H $[\alpha]_{\text{D}}^{24} +47.5$ (<i>c</i> 1.12) ^b
15 : R=Me $[\alpha]_{\text{D}}^{26} -39.70$ (<i>c</i> 0.605) ^b		16 : R=Me $[\alpha]_{\text{D}}^{22} +39.22$ (<i>c</i> 0.995) ^b

^aIsolated yields. ^bMeasured in CHCl₃.

Figure 1. CD spectra of **7** (1.25×10^{-5} mol/dm³) and **8** (1.7×10^{-5} mol/dm³) in methanol.

The asymmetric character of these ligands was examined by circular dichroism (CD) spectroscopy (Fig. 1). Chiral ligands **7** and **8** in methanol show negative and positive bands, respectively, clearly exhibiting a pair of enantiomers. A rather weak exciton coupling at 261 nm in each case indicates that the two pyridine chromophores in **7** and **8** are not in a close relationship to each other, probably due to the conformational flexibility of the side chain. In an effort to understand the possible conformation of these ligands NOE experiments were performed (Fig. 2), and a strong interaction between the C-3 protons on the pyridine ring and the benzylic methylene protons (H_A or H_B) was characterized. Computational techniques using semiempirical molecular mechanics calculations were also applied for conformational analysis of **7**;¹² the most favorable conformer deduced was an extended open chain structure as illustrated in Fig. 3.

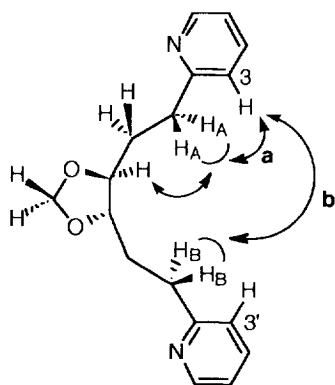


Figure 2. Selected NOE correlations for **7**. The molecule has a 2-fold symmetry, but only one set of NOEs is shown for clarity.

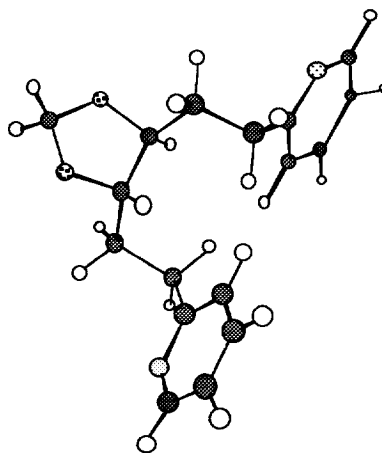
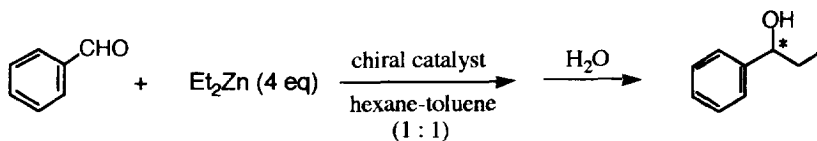


Figure 3. The most stable conformer of **7** calculated with PM3.

These results clearly indicate that the pyridine proton H-3 is in proximity of both H_A and H_B protons; the H_B protons are closer to H-3 than to H-3'. However, due to the C₂-symmetric nature of this ligand these NOE interactions (**a** and **b**) are indistinguishable. Anyway, chiral pyridine derivatives prepared in this work appear to act as a novel bidentate ligand having a relatively large coordination cavity.

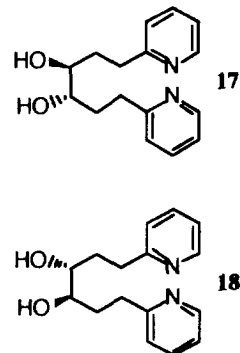
With these results in hand, we then proceeded with the experiments to elucidate the utility of our new ligands for asymmetric synthesis. As the simplest example, enantioselective addition of diethylzinc to benzaldehyde was examined (Scheme 3, Table 2).¹³ Since the use of protected chiral pyridines **7-10** themselves was proved to be ineffective, the corresponding diols **17** and **18**, readily accessible from **9** and **10** by deprotection of an acetonide function, were employed. The reactions in the presence of 10 mol % of **18** in hexane-toluene resulted in unexpectedly low chiral induction, and the addition of Ti(O*i*-Pr)₄ to the system was also fruitless, albeit showing the reverse selectivity. Finally, when Ti(O*i*-Pr)₄ was replaced with Ti(O*t*-Bu)₄, there was a considerable improvement in enantioselectivity (up to 41% ee).¹⁴



Scheme 3

Table 2. Enantioselective Addition of Diethylzinc to Benzaldehyde in the Presence of Chiral Diol **17** or **18**.^a

Catalyst (eq)	Metal Alkoxide (eq)	Yield (%) ^b	Ee (%) ^c	Abs. Config. ^d
18 (0.1)	—	83 ^c	19	<i>S</i>
18 (0.2)	Ti(O <i>i</i> -Pr) ₄ (1.2)	87	18	<i>R</i>
18 (0.1)	Ti(O <i>t</i> -Bu) ₄ (1.2)	89	25	<i>S</i>
18 (0.2)	Ti(O <i>t</i> -Bu) ₄ (1.2)	92	41	<i>S</i>
17 (0.2)	Ti(O <i>t</i> -Bu) ₄ (1.2)	91	40	<i>R</i>
18 (0.5)	Ti(O <i>t</i> -Bu) ₄ (1.2)	94	33	<i>S</i>
18 (1.0)	Ti(O <i>t</i> -Bu) ₄ (1.2)	93	9	<i>S</i>



^aUnless otherwise noted all reactions were conducted at room temperature for 2 days. ^bIsolated yields. ^cDetermined by HPLC (DAICEL Chiralcel OB).

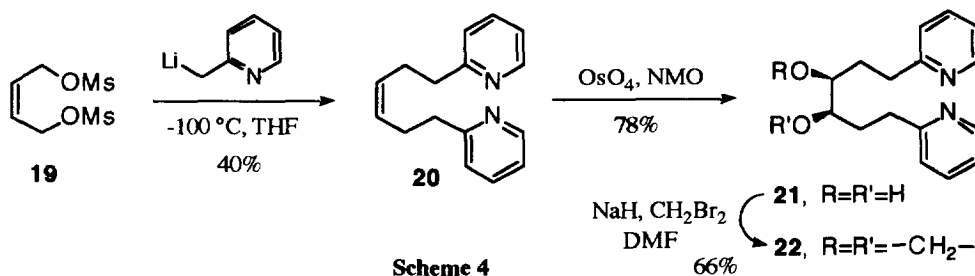
^dDetermined by optical rotation. ^eFor 3 days.

To account for the lower efficiency in the above transformations, it was concluded that the stereogenic centers in **17** and **18** are rather far from the chelating nitrogen atoms and that complexation between chiral ligands and metal alkoxides might be destabilized in solution. We are continuing with the study to improve the enantioselectivity by varying the chiral environment around pyridine nuclei.

Finally, in relation with our effort to design C₂-symmetric pyridine derivatives, we were also interested in the construction of the corresponding *meso*-isomer. Although initial attempts using coupling reaction of triflates

derived from *meso*-tartaric acid were unsuccessful, we found that the desired compound was obtained by employing a completely different approach in which OsO₄-promoted *cis*-dihydroxylation was used to establish the required stereochemistry (Scheme 4).

Thus, treatment of dimesylate **19**¹⁵ with 2 eq of 2-picolylithium at -100 °C⁹ provided **20** in 40% yield. *cis*-Dihydroxylation with OsO₄ followed by protection with CH₂Br₂ gave the desired *meso*-isomer **22** in 52% yield. Extension of this strategy to the field of coordination and supramolecular chemistry is our future program.



In conclusion, we succeeded in developing a general procedure to synthesize all three possible stereoisomers of didentate pyridine derivative ligands **4**. Particularly noteworthy is the ready accessibility of optically active derivatives by taking advantage of sufficient reactivity of chiral triflates. The only unsatisfactory result was the low enantioselectivity in asymmetric induction using chiral ligands **17** and **18**. Apart from this drawback, we believe that the results will be valuable for designing other types of ligands which can be utilized as artificial catalysts or molecular devices.¹⁶ Further studies are now in progress along this line.

Experimental

General Procedure.

All melting points and boiling points are uncorrected. ¹H NMR spectra were recorded on a Hitachi R-90H spectrometer (90 MHz for ¹H NMR analysis and 22.6 MHz for ¹³C NMR analysis) in CDCl₃ solution and are reported in parts per million (δ) downfield from TMS (δ = 0) or CDCl₃ (δ = 77.0) as an internal standard. The FT-IR spectra were measured with a JASCO Model FT/IR-5300 Fourier transform infrared spectrometer and were reported in wavenumbers (cm⁻¹). CD spectra and optical rotations were recorded on a JASCO J-720 spectropolarimeter and a JASCO DIP-370 polarimeter, respectively. Thin-layer chromatography (TLC) was conducted using Merck Kieselgel 60F-254 plates (0.254 mm). Preparative TLC was carried out on 2-mm-thick Merck Kieselgel 60PF-254. Column chromatography was done on Wakogel C-300 and for flash chromatography, Merck Kieselgel (230-240 mesh) was employed.

All reactions were performed in oven-dried glassware under a positive pressure of nitrogen or argon. Air- and moisture-sensitive compounds were introduced via syringe or cannula through a rubber septum. All solvents were dried immediately before use. Et₂O, toluene, and tetrahydrofuran (THF) were distilled from sodium/benzophenone ketyl; acetonitrile and *N,N*-dimethylformamide (DMF) were distilled from CaH₂. Starting ditriflates **1** and **2** were prepared by conventional treatment of the parent diol with triflic anhydride in

pyridine.¹⁷ $\text{Ti}(\text{O}i\text{-Bu})_4$ was prepared from $\text{Ti}(\text{O}i\text{-Pr})_4$ according to the literature procedure¹⁸ and used after vacuum distillation.

Physical data of chiral ligands are shown only for *S,S*-enantiomers; completely the same results were obtained for *R,R*-isomers except for specific rotations.

(2*S*, 3*S*)-2,3-Methylenedioxybutane-1,4-diol (1).

A solution of dimethyl L-tartrate (80 g, 0.45 mol), paraformaldehyde (35g, 1.2 mol) and catalytic amounts of *p*-TsOH in benzene (540 mL) was refluxed for 2 days.¹⁹ The mixture was concd to give a crude product which was distilled at 122 °C / 0.25 mmHg to give the corresponding methylenedioxy ester (37 g, 43%) as a colorless oil. To a suspension of LiAlH_4 (11g, 0.29 mol) in 600 mL of Et_2O at 0 °C was added a solution of this ester in 300 mL of Et_2O . After stirring for 10 h, the mixture was quenched with aq KOH followed by extraction with AcOEt. The extracts were concd to give a crude product which was distilled at 85 °C / 0.1 mmHg to give *S,S*-**1** (14.3 g, 58%) as a colorless oil: R_f 0.08 (Et_2O); $[\alpha]_D^{27}$ -29.51 (*c* 0.61, MeOH) {lit.²⁰ $[\alpha]_{546}^{20}$ -30.0 (*c* 0.1, MeOH)}.

Similarly, *R,R*-**1** was also prepared from dimethyl D-tartrate: $[\alpha]_D^{27}$ +29.70 (*c* 0.61, MeOH).

Preparation of Optically Active C_2 -Symmetric Pyridine Derivatives. As a typical example, the procedure to obtain **9** is described as follows. To a solution of LDA (44.7 mmol) in THF (51 mL) at -78 °C was added dropwise 2-picoline (4.4 mL, 44.7 mmol) and the mixture was warmed to 0 °C. After stirring for 1 h, the mixture was recooled to -100 °C and dinitrile **2** (12.33 mmol)¹⁷ in THF (20 mL) was introduced slowly and the mixture was stirred at this temperature for 1 h. The mixture was quenched with aq KOH and the formed insoluble substance was removed by filtration through Celite. After extraction with AcOEt, the crude product was purified by silica gel column chromatography (hexane/acetone, 1:1) to afford **9** (3.43 g, 80%) as a pale yellow oil. Specific rotations for the compounds prepared by this method are listed in Table 1.

(3*S*, 4*S*)-1,6-Bis(2-pyridyl)-3,4-*O*-methylene-3,4-dihydroxyhexane (7). Oil; bp 210 °C/0.11 mmHg (bath temperature); R_f 0.29 (benzene/acetone, 2 : 1); FTIR (neat) ν 1591, 1570, 1476, 1435, 1152, 1088, 992, 752; ^1H NMR δ 2.03 (4H, m), 2.94 (4H, m), 3.67 (2H, mt, $J = 4.4$ Hz), 5.01 (2H, s), 6.9-7.2 (4H, m), 7.57 (2H, br t, $J = 7.4$ Hz), 8.51 (2H, br d, 2H, $J = 4.4$ Hz); ^{13}C NMR δ 31.97 ($\times 2$), 34.13 ($\times 2$), 80.05 ($\times 2$), 93.53, 120.60 ($\times 2$), 122.34 ($\times 2$), 135.75 ($\times 2$), 148.71 ($\times 2$), 160.57 ($\times 2$); MS m/z (rel intensity) 284 ($M^+ + 1$), 253 (3), 237 (13), 192 (94), 162 (78), 146 (20), 130 (8), 118 (29), 106 (28), 93 (100), 78 (7), 65 (5), 32 (28). HRMS calcd for $\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}_2$ 284.1525, found 284.1505.

(3*S*, 4*S*)-1,6-Bis(2-pyridyl)-3,4-*O*-isopropylidene-3,4-dihydroxyhexane (9). Pale yellow oil; R_f 0.35 (benzene/acetone, 2 : 1); FTIR (neat) ν 1591, 1570, 1476, 1435, 1377, 1240, 1096, 1055, 995, 870; ^1H NMR δ 1.41 (6H, s), 2.02 (4H, m), 2.93 (4H, m), 3.72 (2H, m), 6.9-7.3 (4H, m), 7.57 (2H, dt, $J = 7.5$, 2.0 Hz), 8.50 (2H, br d, $J = 4.8$ Hz); ^{13}C NMR δ 27.42 ($\times 2$), 32.67 ($\times 2$), 34.71 ($\times 2$), 80.29 ($\times 2$), 108.16, 120.97 ($\times 2$), 122.77 ($\times 2$), 136.15 ($\times 2$), 149.17 ($\times 2$), 161.30 ($\times 2$); MS m/z (rel intensity) 313 ($M^+ + 1$, 1), 297 (90), 255 (23), 237 (22), 220 (53), 162 (100), 144 (20), 119 (50), 106 (27), 93 (68), 78 (7), 65 (6), 43 (6), 32 (7). HRMS calcd for $\text{C}_{19}\text{H}_{24}\text{N}_2\text{O}_2$ 312.1838, found 312.1832.

(3S, 4S)-1,6-Bis(6-methyl-2-pyridyl)-3,4-O-methylene-3,4-dihydroxyhexane (11). Yellow oil; bp 231 °C/0.2 mmHg (bath temperature); *R*_f 0.34 (benzene/acetone, 2:1); FTIR (neat) ν 1593, 1578, 1458, 1157, 1090; ¹H NMR δ 2.00 (4H, m), 2.50 (6H, s), 2.90 (4H, m), 3.66 (2H, mt, *J* = 4.4 Hz), 5.00 (s, 2H), 6.94 (4H, d, *J*=7.4 Hz), 7.45 (2H, t, *J*=7.4 Hz); ¹³C NMR δ 24.37 (\times 2), 32.61 (\times 2), 34.56 (\times 2), 80.48 (\times 2), 93.83, 119.47 (\times 2), 120.39 (\times 2), 136.30 (\times 2), 157.58 (\times 2), 160.27 (\times 2); MS *m/z* (rel intensity) 312 (M⁺, 2), 282 (8), 267 (10), 206 (48), 176 (59), 160 (10), 132 (15), 120 (24), 107 (100), 92 (4), 77 (3), 65 (3), 40 (3), 32 (38). HRMS calcd for C₁₉H₂₄N₂O₂ 312.1838, found 312.1826.

(3S, 4S)-1,6-Bis(2,2'-bipyridyl-6-yl)-3,4-O-methylene-3,4-dihydroxyhexane (13). Orange oil; *R*_f 0.50 (AcOEt containing a drop of Et₃N); FTIR (neat) ν 1580, 1458, 1429, 1152, 1088, 990, 779; ¹H NMR δ 2.16 (4H, m), 3.02 (4H, m), 3.78 (2H, m), 5.05 (2H, s), 7.17 (4H, m), 7.68 (4H, t, *J* = 7.7 Hz), 8.21 (2H, d, *J* = 7.7 Hz), 8.40 (2H, d, *J* = 7.7 Hz), 8.63 (2H, br d, *J* = 4.0 Hz); ¹³C NMR δ 32.18 (\times 2), 34.44 (\times 2), 80.63 (\times 2), 93.98, 118.34 (\times 2), 121.06 (\times 2), 122.80 (\times 2), 123.38 (\times 2), 136.61 (\times 2), 137.03 (\times 2), 148.90 (\times 2), 155.42 (\times 2), 156.30 (\times 2), 160.30 (\times 2); MS *m/z* (rel intensity) 438 (M⁺, 1), 408 (4), 390 (14), 269 (44), 239 (32), 223 (10), 195 (14), 183 (24), 170 (100), 155 (5), 117 (2), 78 (3), 32 (18). HRMS calcd for C₂₇H₂₆N₄O₂ 438.2056, found 438.2065.

(3S, 4S)-1,6-Bis(2,2'-bipyridyl-6-yl)-3,4-O-isopropylidene-3,4-dihydroxyhexane (15). Pale orange oil; *R*_f 0.58 (AcOEt containing a drop of Et₃N); FTIR (neat) ν 1582, 1429, 1377, 1240, 1094, 993, 868, 779; ¹H NMR δ 1.45 (6H, s), 2.15 (4H, m), 3.02 (4H, m), 3.83 (2H, mt, *J* = 3.5 Hz), 7.16 (4H, m), 7.65 (4H, t, *J* = 7.7 Hz), 8.17 (2H, d, *J* = 7.7 Hz), 8.38 (2H, d, *J* = 7.9 Hz), 8.60 (2H, d, *J* = 4.6 Hz); ¹³C NMR δ 27.30 (\times 2), 32.15 (\times 2), 34.28 (\times 2), 80.11 (\times 2), 107.83, 118.04 (\times 2), 120.78 (\times 2), 122.55 (\times 2), 123.13 (\times 2), 136.30 (\times 2), 136.70 (\times 2), 148.65 (\times 2), 155.11 (\times 2), 156.06 (\times 2), 160.27 (\times 2); MS *m/z* (rel intensity) 467 (M⁺ + 1, 100), 451 (9), 437 (11), 409 (28), 390 (6), 297 (11), 239 (14), 195 (5), 183 (5), 170 (19), 41 (3). HRMS calcd for C₂₉H₃₀N₄O₂ + H 467.2447, found 467.2432.

(3S, 4S)-1,6-Bis(2-pyridyl)-hexane-3,4-diol (17).

A solution of **9** (100 mg, 0.35 mmol) in 3.0 mL of 5% aq CH₃CN containing 90 μ L (0.53 mmol) of 6M HCl was stirred at rt for 17 h. The mixture was diluted with 2M HCl and extracted with Et₂O to remove a neutral fraction. The aqueous phase was basified with aq NaOH and extracted thoroughly with AcOEt. The extracts were dried (Na₂SO₄) and concd. The crude product was purified by silica gel column chromatography (AcOEt/MeOH, 9: 1) and then recrystallized from Et₂O to give **17** (88 mg, 92%) as a white powder: mp 69.5-70.0 °C; *R*_f 0.38 (CH₂Cl₂/MeOH, 9: 1); [α]_D²³ -13.98 (*c* 1.07, CHCl₃); FTIR (KBr) ν 3351, 1595, 1480, 1437, 1073, 772; ¹H NMR δ 2.03 (4H, m), 3.00 (4H, t, *J* = 7.0 Hz), 3.50 (2H, m), 4.00 (2H, br), 6.9-7.3 (4H, m), 7.59 (2H, dt, *J* = 7.5, 1.8 Hz), 8.47 (2H, br d, *J* = 4.2 Hz); ¹³C NMR δ 32.64 (\times 2), 34.53 (\times 2), 74.04 (\times 2), 121.09 (\times 2), 123.22 (\times 2), 136.67 (\times 2), 148.50 (\times 2), 161.58 (\times 2). Calcd for C₁₆H₂₀N₂O₂ C, 70.56; H, 7.40; N, 10.29, found C, 70.70, H, 7.48, N, 10.11.

Similarly, **18** was also obtained from **10**: [α]_D²⁵ +13.82 (*c* 1.01, CHCl₃).

General Procedure for Enantioselective Addition of Diethylzinc to Benzaldehyde.

To a solution of chiral ligand **17** or **18** and 1.13 mmol of $\text{Ti}(\text{OR})_4$ in toluene (4 mL) at $-15\text{ }^\circ\text{C}$ was added 3.88 mL of Et_2Zn (3.76M in hexane) and the resulting yellow solution was stirred for 15 min at this temperature. Then, benzaldehyde (96 μL , 0.94 mmol) was introduced at $-15\text{ }^\circ\text{C}$ and the mixture was allowed to warm to rt and stirred for 2 to 3 days. After quenching with 1M HCl, the insoluble substance was removed by filtration through Celite. The filtrate was extracted with AcOEt and dried (Na_2SO_4). Evaporation of the solvent gave a crude product which was purified by preparative TLC (petroleum ether/AcOEt, 5 : 1) to give 1-phenyl-1-propanol as a colorless oil. The enantiomeric excess (ee) of the product was determined by Hitachi L-6200 HPLC using a DAICEL Chiralcel OB column eluted with 1% 2-propanol in hexane.

***cis*-1,6-Dipyridyl-3-hexene (20).**

To a solution of LDA (9.4 mmol) in 9 mL of THF at $-78\text{ }^\circ\text{C}$ was added 2-picoline (924 μL , 9.4 mmol) and the mixture was stirred for 30 min at $0\text{ }^\circ\text{C}$. Then, a solution of dimesylate **19** (765 mg, 3.13 mmol)¹⁵ in 2 mL of THF at $-100\text{ }^\circ\text{C}$ was introduced and the mixture was stirred at this temperature for 1 h. The mixture was quenched with aq KOH followed by filtration. The filtrate was concd and the residue was extracted with AcOEt. Evaporation of the solvent gave a crude product which was purified by silica gel column chromatography (benzene/acetone, 4 : 1) to give **20** (298 mg, 40%) as a pale yellow oil: R_f 0.32 (benzene/acetone, 2 : 1); FTIR (neat) ν 1591, 1568, 1476, 1435, 1150, 1051, 993, 750; ^1H NMR δ 2.3-2.6 (4H, m), 2.6-3.0 (4H, m), 5.43 (2H, t, $J = 4.4$ Hz), 6.9-7.2 (4H, m), 7.56 (2H, dt, $J = 7.9, 2.0$ Hz), 8.50 (2H, br d, $J = 4.5$ Hz); ^{13}C NMR δ 27.42 ($\times 2$), 38.16 ($\times 2$), 120.91 ($\times 2$), 122.80 ($\times 2$), 129.32 ($\times 2$), 136.09 ($\times 2$), 149.02 ($\times 2$), 161.43 ($\times 2$); MS m/z (rel intensity) 238 (M^+ , 1), 209 (1), 146 (100), 130 (6), 117 (15), 106 (3), 93 (38), 78 (3), 65 (6), 51 (2), 39 (3), 32 (6). HRMS calcd for $\text{C}_{16}\text{H}_{18}\text{N}_2$ 238.1470, found 238.1465.

***meso*-1,6-Bis(2-pyridyl)-hexane-3,4-diol (21).**

To a solution of **20** (650 mg, 2.73 mmol) in H_2O (7 mL) and acetone (3.5 mL) were added NMO (316 mg, 2.7 mmol) and OsO_4 (1 mg), and the mixture was stirred at rt for 12 h. After quenching with aq $\text{Na}_2\text{S}_2\text{O}_3$, florisil was added and the insoluble substance was removed by filtration through Celite. The filtrate was extracted with AcOEt and dried (Na_2SO_4). Evaporation of the solvent gave a crude product which was recrystallized from hexane- CH_2Cl_2 to give diol **21** as colorless needles (580 mg, 78%): mp $123.0\text{--}125.0\text{ }^\circ\text{C}$; R_f 0.06 (benzene/acetone, 2 : 1) FTIR (KBr) ν 3210, 1595, 1568, 1476, 1449, 1074, 1046, 1003, 845, 768; ^1H NMR δ 2.04 (4H, m), 3.04 (4H, t, $J = 6.8$ Hz), 3.63 (2H, m), 4.75 (2H, br s), 6.9-7.3 (4H, m), 7.60 (2H, dt, $J = 7.6, 1.8$ Hz), 8.46 (2H, br d, $J = 4.8$ Hz); ^{13}C NMR δ 31.02 ($\times 2$), 34.68 ($\times 2$), 74.35 ($\times 2$), 121.03 ($\times 2$), 123.25 ($\times 2$), 136.73 ($\times 2$), 148.32 ($\times 2$), 161.67 ($\times 2$). Calcd for $\text{C}_{16}\text{H}_{20}\text{N}_2\text{O}_2$ C, 70.56; H, 7.40; N, 10.29, found C, 70.42, H, 7.37, N, 10.23.

***meso*-3,4-Methylenedioxy-1,6-bis(2-pyridyl)-hexane (22).**

To a suspension of NaH (60% dispersion in oil; 200 mg, 5 mmol) in DMF (2 mL) at $0\text{ }^\circ\text{C}$ was added diol **21** (580 mg, 2.13 mmol) in DMF (5 mL). After stirring for 15 min, CH_2Br_2 (170 μL , 2.43 mmol) was added and the mixture was stirred at rt for 2 h. After quenching with H_2O , the insoluble substance was removed by filtration through Celite. The filtrate was concd and the residue was extracted with AcOEt. Evaporation of the solvent gave a crude product which was purified by silica gel column chromatography (benzene/acetone, 4 : 1) to give **22** (402 mg, 66%) as a pale yellow oil: R_f 0.48 (benzene/ acetone, 2 : 1); FTIR (neat) ν 1593, 1568, 1476,

1435, 1092, 993, 752; ¹H NMR δ 1.96 (4H, m), 2.95 (4H, m), 3.98 (2H, m), 4.85, 5.15 (each 1H, s), 7.15 (4H, m), 7.57 (2H, dt, *J* = 7.7, 1.8 Hz), 8.51 (2H, br d, *J* = 4.4 Hz); ¹³C NMR δ 29.19 (× 2), 34.89 (× 2), 77.37 (× 2), 93.80, 120.97 (× 2), 122.83 (× 2), 136.15 (× 2), 149.14 (× 2), 161.15 (× 2); MS *m/z* (rel intensity) 285 (*M*⁺ + 1, 2), 253 (2), 239 (12), 192 (63), 162 (60), 146 (20), 130 (20), 118 (37), 106 (39), 93 (100), 78 (10), 65 (7), 51 (4), 32 (5). HRMS calcd for C₁₇H₂₀N₂O₂ + H 285.1603, found 285.1631.

Acknowledgments. One of the authors (H.K.) acknowledges the financial support of this work by the Tanabe Seiyaku Award in Synthetic Organic Chemistry and CIBA-GEIGY Foundation (Japan) for the Promotion of Science. We are grateful to Prof. Y. Fukuyama of Tokushima Bunri University for MS/HRMS measurements and to Dr. T. Yonemura of our University for CD measurements. We wish to thank Central Glass Co., Ltd. for a generous supply of triflic anhydride.

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(Received in Japan 16 March 1995)