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New Convenient, Enantiospecific Synthesis of (*S,S*)- and (*R,R*)-2,2'-Bipyrrolidine Derivatives#

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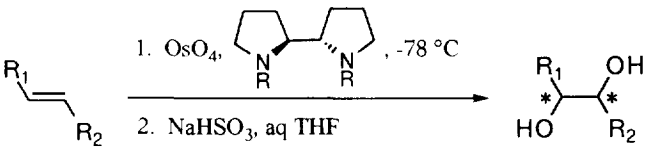
Abstract: An enantiomeric pair of (*S,S*)- and (*R,R*)-bipyrrolidine derivatives has been prepared from D- and L-tartaric acids or D-mannitol as optically active starting materials. Taking advantage of the C_2-symmetric nature of these chiral sources, the synthetic sequence has been established by using efficient side chain elongation, stereospecific conversion of a vicinal diol into a diazido group via S_N2 inversion, and pyrrolidine ring formation via intramolecular substitution as the key steps.

In recent years a great deal of success has been achieved in the field of catalytic asymmetric synthesis, in which the development of effective chiral catalysts plays an essential role. Accordingly, a variety of catalytic systems employing new chiral ligands have been reported.[1] Among them, nitrogen containing ligands exhibit a potentially versatile utility,[2] and chiral vicinal diamine derivatives have gained particular attention, since they are useful not only as powerful coordinating ligands for asymmetric synthesis[3, 4] but also as chiral auxiliaries,[5] chiral reagents,[6] chiral solvating agents,[7] and chiral architectural elements for supramolecular chemistry.[8]

Our continuing interest in utilizing tartaric acid as a chiral source[9] for the synthesis of optically active natural products[10] and also for the elaboration of novel chiral ligands[11] focused our attention on the efficient construction of C_2-symmetric bipyrrolidine derivatives. These ligands were originally developed for an osmium tetroxide-promoted asymmetric dihydroxylation of olefins (Eq. 1)[4] and their synthetic approach relied on chiral resolution of racemic compounds.[12]



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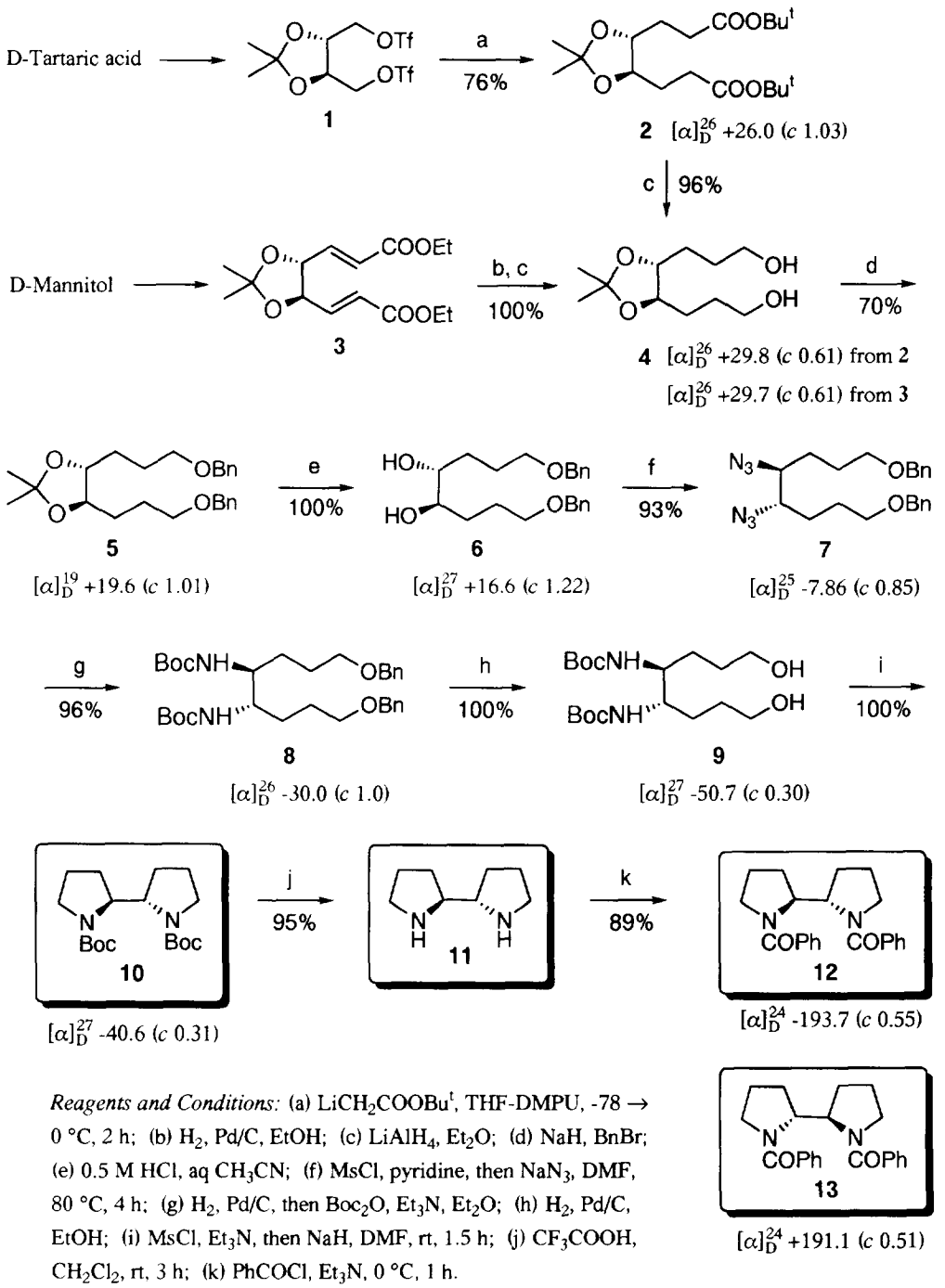
#Dedicated to Prof. T. Tokoroyama upon his retirement from Osaka City University.



Reagents and Conditions: (a) $LiCH_2COOBu^t$, THF-DMPU, -78 → 0 °C, 2 h; (b) H_2, Pd/C, EtOH; (c) $LiAlH_4$, Et_2O; (d) NaH, BnBr; (e) 0.5 M HCl, aq CH_3CN; (f) MsCl, pyridine, then NaN_3, DMF, 80 °C, 4 h; (g) H_2, Pd/C, then Boc_2O, Et_3N, Et_2O; (h) H_2, Pd/C, EtOH; (i) MsCl, Et_3N, then NaH, DMF, rt, 1.5 h; (j) CF_3COOH, CH_2Cl_2, rt, 3 h; (k) PhCOCl, Et_3N, 0 °C, 1 h.

Scheme 1. Enantiospecific synthesis of 2,2'-bipyrrolidine derivatives. Specific rotations were measured in $CHCl_3$.

Our synthetic strategy is based upon our own protocol using carbon-carbon bond forming reactions at the carbon centers bearing β-oxygen atoms via triflate intermediates.[10] Taking advantage of the vicinal diol system of tartaric acid or D-mannitol, stereospecific construction of a diazido functionality was designed to establish the required stereochemistry.[13] These approaches should permit us to reach the target molecules in a straightforward way without involving any racemization or epimerization steps. We now report a new and convenient method of synthesizing optically active C_2-symmetric bipyrrolidine derivatives using this strategy.

As outlined in Scheme 1, starting with D-tartaric acid, diester **2** was obtained by an efficient coupling reaction of ditriflate **1**[10a] with 2.5 equiv. of a lithio anion of *tert*-butyl acetate in 76% yield.[10j] Subsequent reduction with $LiAlH_4$ afforded diol **4** in 96% yield. The same compound was also prepared quantitatively from **3**, readily available from D-mannitol,[14] by a two-step sequence: 1. hydrogenation on Pd/C, and 2. $LiAlH_4$ reduction of diethyl ester. Conventional treatment of **4** with NaH and benzyl bromide followed by deprotection of an acetonide function provided diol **6** in high yield.

Stereospecific construction of the required vicinal diamine equivalent was then examined by applying S_N2 inversion with azide onto the dimesylate intermediate derived from **6**.[15] Thus, mesylation followed by reaction with 6 equiv. of NaN_3 in DMF at 80 °C gave (*S,S*)-diazido **7** in 93% yield. As pointed out in the literature,[15] the temperature control for this substitution reaction was crucial, e.g., at higher temperatures the yield was considerably decreased and at lower temperatures the reaction was incomplete even after prolonged stirring. Selective catalytic hydrogenation of the diazido group into diamines was achieved cleanly by using Degussa type Pd/C as a catalyst and, after protection with Boc_2O, the diBoc derivative **8** was obtained in 96% yield. Debenzylation under normal conditions provided the diol **9**, mp 147.0-148.0 °C, which was further converted into the corresponding dimesylate. Intramolecular cyclization of this substrate occurred smoothly by treatment with a slightly excess amount of NaH in DMF to furnish (*S,S*)-2,2'-bipyrrolidine **10** in quantitative yield. At this stage, an alternative pathway to form a 6-membered ring compound, a cis-fused diazadecalin homologue, was excluded due to the steric and kinetic inaccessibility. Unambiguous confirmation of this interpretation was verified by X-ray diffraction analysis at a later stage. Finally, **10** was deprotected into the corresponding free diamine **11** by exposure to trifluoroacetic acid. As expected, this diamine **11** was rather sensitive to an ambient atmosphere and was subjected to the subsequent benzoylation without comparing the physical properties with the literature data[13]. Thus, (*S,S*)-1,1'-dibenzoyl-2,2'-bipyrrolidine (**12**), mp 148.0-149.0 °C; $[\alpha]^{24}_D$ -193.7 (*c* 0.55, $CHCl_3$) (lit.[16] mp 149-150 °C; $[\alpha]^{23}_D$ -192 (*c* 1.02, $CHCl_3$)), was isolated in excellent yield as a highly crystalline compound.

Following completely the same synthetic sequence from L-tartaric acid, (*R,R*)-1,1'-dibenzoyl-2,2'-bipyrrolidine (**13**), $[\alpha]^{24}_D$ +191.1 (*c* 0.51, $CHCl_3$), was also prepared as an antipode of **12**. HPLC analyses of **12** and **13** using DAICEL CHIRALCEL OD (hexane/2-propanol, 10 : 1) revealed enantiomeric excesses of 100% and >98%, respectively.

As the final project to confirm the geometrical configuration of these bipyrrolidine derivatives, X-ray diffraction analysis of **13** was performed. In the stereodrawing diagram shown in Figure 1 we can see that the favored conformation in the solid state has a completely anti-form with respect to hydrogen atoms between the two pyrrolidine rings. A spatial arrangement of two benzoyl substituents on nitrogen atoms also contributes to offer a suitable coordinating cavity, implying that a satisfactory asymmetric environment is present around this didentate ligand.[17]

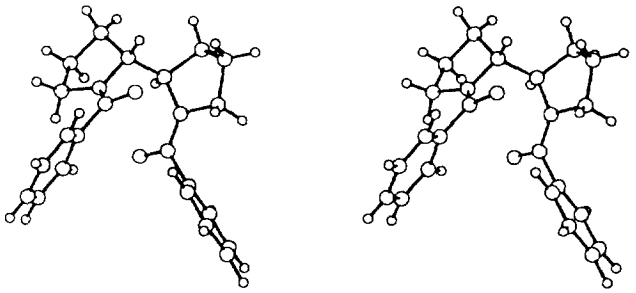


Figure 1. Stereodrawing of the crystal structure of compound **13**.

In conclusion, we have succeeded in developing a convenient procedure to synthesize both enantiomers of 2,2'-bipyrrolidine derivatives such as **10**, **11**, and **12** in an enantiomerically well-defined method. The entire synthetic sequence is quite simple and hence easy to scale up. The overall yield of **10** for the 11-step sequence was 45.6% from **1** and 62.5% from **3**. We believe that the results will be valuable for designing other types of related chiral ligands having a C_2-symmetric character. Further studies are now in progress along this line.

Experimental

General Procedure.

All melting points and boiling points are uncorrected. ^{1}H NMR spectra were recorded on a Hitachi R-90H spectrometer (90 MHz for ^{1}H NMR analysis and 22.6 MHz for ^{13}C NMR analysis) in $CDCl_3$ solution and are reported in parts per million (δ) downfield from TMS (δ = 0) or $CDCl_3$ (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 reported in wavenumbers (cm^{-1}). Optical rotations were recorded on a JASCO DIP-370 polarimeter. Thin-layer chromatography (TLC) was done using Merck Kiesegel 60F-254 plates (0.254 mm). Column chromatography was done on Wakogel C-300.

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. Et_2O and tetrahydrofuran (THF) were distilled from sodium/benzophenone ketyl; *N,N*-diisopropylamine, 1,3-dimethyl-1,3,4,5,6-tetrahydro-2-(1H)-pyrimidinone (DMPU), *tert*-butyl acetate, triethylamine, and *N,N*-dimethylformamide (DMF) were distilled from CaH_2. Starting ditriflates **1** were prepared by conventional treatment of the parent diol with triflic anhydride in pyridine.[10]

Specific rotations of the products obtained from D-tartaric acid or D-mannitol are compiled in Scheme 1. The corresponding enantiomers were also prepared from L-tartaric acid.

Di-*tert*-butyl (4*R*,5*R*)-4,5-(isopropylidene)dioxy-1,8-octanedioate (2).

To a solution of LDA (11.0 mmol), prepared from *i*-Pr_2NH (1.44 mL, 11.0 mmol) and *n*-BuLi (7.54 mL, 1.46 M), in THF (30 mL) at -70 °C was added *tert*-butyl acetate (1.35 mL, 10.0 mmol), and the mixture was stirred at this temperature for 30 min. To the mixture at -78°C was added DMPU (6.8 mL) followed by a

solution of the ditriflate **1** (1.55g, 4.0 mmol) in THF (20 mL), and the mixture was stirred at 0 °C for 2 h. After quenching with satd $NaHCO_3$ and evaporation of most of the organic solvent, the mixture was extracted with Et_2O. The extracts were washed with satd NaCl, dried (Na_2SO_4), and concd. The crude product was purified by silica gel column chromatography (hexane/AcOEt from 10 : 1 to 5 : 1) to afford **2** (1.09 g, 76%) as a colorless oil: FTIR (neat) ν 1730, 1368, 1254, 1154, 1088, 982, 849; ^{1}H NMR ($CDCl_3$) δ 1.35 (6H, s), 1.44 (18H, s), 1.5-2.0 (4H, m), 2.39 (4H, m), 3.62 (2H, m); ^{13}C NMR ($CDCl_3$) δ 27.18 (× 2), 27.82 (× 2), 28.03 (× 6), 31.84 (× 2), 79.56 (× 2), 80.05 (× 2), 108.10, 172.13 (× 2); MS *m/z* (rel intensity) 359 (61, M^+ + 1), 303 (42), 287 (4), 247 (100), 231 (31), 217 (19), 199 (8), 189 (37), 171 (53), 153 (5), 57 (6), 42 (8). HRMS calcd for $C_{19}H_{34}O_6$ + H 359.2434, found 359.2409.

The *S,S*-enantiomer: $[\alpha]^{26}_D$ -26.1 (*c* 1.02, $CHCl_3$).

(4*R*,5*R*)-4,5-(Isopropylidene)dioxy-1,8-octanediol (4).

From 2: To a suspension of $LiAlH_4$ (96 mg, 2.53 mmol) in Et_2O (8 mL) at 0 °C was added dropwise diester **2** (605 mg, 1.69 mmol) in Et_2O (5 mL) and the mixture was stirred at rt for 2 h. After quenching with water (0 °C), the mixture was filtered through Celite and washed thoroughly with AcOEt. Evaporation of the solvent gave a crude product which was purified by silica gel column chromatography (AcOEt) to give diol **4** as a colorless oil (354 mg, 96%): R_f 0.38 (AcOEt/MeOH, 10 : 1); FTIR (neat) ν 3374, 1447, 1377, 1063; ^{1}H NMR ($CDCl_3$) δ 1.39 (6H, s), 1.5-1.9 (8H, m), 2.37 (2H, s), 3.67 (6H, m); ^{13}C NMR ($CDCl_3$) δ 27.21 (× 2), 29.22 (× 4), 62.21 (× 2), 80.69 (× 2), 108.01; MS *m/z* (rel intensity) 219 (4, M^+ + 1), 203 (24), 161 (10), 143 (100), 130 (18), 125 (17), 107 (8), 101 (8), 97 (12), 81 (9), 71 (21), 59 (21), 55 (10), 43 (11). HRMS calcd for $C_{11}H_{22}O_4$ + H 219.1596, found 219.1583.

From 3: A solution of diester **3** (790 mg, 2.65 mmol) in abs EtOH (20 mL) containing 5% Rh-C (70 mg) was stirred vigorously under H_2 atmosphere until consumption of the starting material by monitoring on TLC (overnight). Removal of the catalyst by filtration through Celite followed by concentration provided a crude diester, which was dissolved in Et_2O (10 mL) and treated with $LiAlH_4$ (122 mg, 3.2 mmol) in Et_2O (10 mL) at 0 °C. After stirring overnight at rt, the mixture was quenched with a minimum amount of aq KOH. The insoluble substance formed was removed by filtration through Celite and rinsed well with AcOEt. The filtrate was concd in vacuo and the residue was purified by silica gel column chromatography (AcOEt/MeOH, 10 : 1) to give diol **4** (580 mg, 100%) as a colorless oil.

The *S,S*-enantiomer: $[\alpha]^{19}_D$ -29.8 (*c*1.02, $CHCl_3$).

(4*R*,5*R*)-4,5-(Isopropylidene)dioxy-1,8-octanediol dibenzyl ether (5).

To a solution of NaH (60% dispersion in oil; 1.35 g, 33.8 mmol) in THF (20 mL) at 0 °C was added diol **4** (2.97 g, 13.6 mmol) in THF (20 mL) and the mixture was stirred for 30 min. Then benzyl bromide (4.0 mL, 33.6 mmol) was introduced and the mixture was stirred at rt overnight. After quenching with aq NH_4Cl followed by evaporation of most of the organic solvent, the residue was extracted with AcOEt. The extracts were washed with satd $NaHCO_3$ and satd NaCl, dried (Na_2SO_4), and concd. The crude product was purified by silica gel column chromatography (hexane/AcOEt from 5 : 1 to 2 : 1) to afford dibenzyl ether **5** (3.8 g, 70%) as a colorless oil: R_f 0.40 (hexane/AcOEt, 2 : 1); FTIR (neat) ν 1454, 1368, 1242, 1098, 737, 698; ^{1}H NMR ($CDCl_3$) δ 1.35 (6H, s), 1.4-2.0 (8H, m), 3.49 (6H, m), 4.49 (4H, s), 7.31 (10H, s); ^{13}C NMR ($CDCl_3$) δ 26.33 (× 2), 27.36 (× 2), 29.56 (× 2), 70.05 (× 2), 72.82 (× 2), 80.60 (× 2), 107.79, 127.37 (× 2), 127.49 (×

4), 128.22 (× 4), 138.45 (× 2); MS *m/z* (rel intensity) 398 (0.4, M^+), 383 (8), 249 (2), 233 (4), 181 (10), 143 (41), 91 (100), 71 (35), 59 (4), 43 (5). HRMS calcd for $C_{25}H_{34}O_4$ 398.2457, found 398.2366.

The *S,S*-enantiomer: $[\alpha]^{26}_D$ -19.6 (*c* 1.12, $CHCl_3$).

(4*R*,5*R*)-1,8-Dibenzyloxy-4,5-octanediol (6).

A stirred solution of dibenzyl ether **5** (360 mg, 0.9 mmol) in 5% aq CH_3CN (14 mL) was treated with 0.5 M HCl (2 mL) at rt for 8 h. After removal of the solvent, the residue was extracted with AcOEt. The extracts were washed with satd NaCl, dried (Na_2SO_4), and concd. The crude product was purified by silica gel column chromatography (AcOEt) to give diol **6** (324 mg, 100%) as a colorless oil: R_f 0.15 (AcOEt); FTIR (neat) ν 3416, 1454, 1364, 1100, 739, 698; ^1H NMR ($CDCl_3$) δ 1.4-1.9 (8H, m), 2.80 (2H, s), 3.51 (6H, m), 4.50 (4H, s), 7.31 (10H, s); ^{13}C NMR ($CDCl_3$) δ 26.05 (× 2), 30.78 (× 2), 70.38 (× 2), 72.91 (× 2), 74.07 (× 2), 127.55 (× 6), 128.25 (× 4), 138.07 (× 2).

The *S,S*-enantiomer: $[\alpha]^{26}_D$ -16.8 (*c* 1.31, $CHCl_3$).

(4*S*,5*S*)-4,5-Diazido-1,8-octanediol dibenzyl ether (7).

To a solution of diol **6** (5.23 g, 14.6 mmol) and Et_3N (16.3 mL, 117 mmol) in CH_2Cl_2 (280 mL) at 0 °C was added MsCl (8.36 g, 73.0 mmol) and the mixture was stirred at rt for 10 min. After dilution with CH_2Cl_2, the organic layer was washed with 5% aq $CuSO_4$, water, satd $NaHCO_3$, and satd NaCl, and dried (Na_2SO_4). Evaporation of the solvent gave a crude dimesylate.

A mixture of this product and NaN_3 (5.65 g, 87 mmol) in DMF (100 mL) was stirred at 80 °C for 4 h. After removal of most of the organic solvent, the residue was poured into satd NaCl and extracted with AcOEt. The extracts were dried (Na_2SO_4) and concd. The crude product was purified by silica gel column chromatography (hexane/AcOEt , from 5 : 1 to 2 : 1) to give diazido **7** (5.53 g, 93%) as a colorless oil: R_f 0.57 (hexane/AcOEt, 1 : 1); FTIR (neat) ν 2101, 1454, 1360, 1260, 1101, 737, 698; ^1H NMR ($CDCl_3$) δ 1.72 (8H, s), 3.2-3.6 (6H, m), 4.49 (4H, s), 7.31 (10H, s); ^{13}C NMR ($CDCl_3$) δ 26.39 (× 2), 28.37 (× 2), 65.11 (× 2), 69.47 (× 2), 72.98 (× 2), 127.55 (× 6), 128.28 (× 4), 138.25 (× 2); MS *m/z* (rel intensity) 409 (0.2, $M^+ + 1$), 381 (2), 353 (6), 338 (6), 268 (3), 245 (3), 217 (5), 176 (10), 160 (2), 119 (7), 91 (100), 71 (9), 70 (10), 41 (28). HRMS calcd for $C_{22}H_{28}N_6O_2$ + H 409.2352, found 409.2357.

The *R,R*-enantiomer: $[\alpha]^{26}_D$ +7.86 (*c* 0.84, $CHCl_3$).

(4*S*,5*S*)-4,5-Di(*tert*-butoxycarbonylamino)-1,8-octanediol dibenzyl ether (8).

A mixture of diazido **7** (8.81 g, 21.6 mmol) in abs EtOH (300 mL) containing 500 mg of Pd on activated carbon (wet, Degussa type E 101 NE/W) was stirred at rt under H_2 atmosphere. After completion of the reaction (4 h), the mixture was filtered through Celite and concd. The residue was dissolved in Et_2O (500 mL) and treated with Et_3N (12 mL, 86 mmol) and Boc_2O (28.3 g, 130 mmol) under refluxing overnight. Then the mixture was concd and purified by silica gel column chromatography (hexane/AcOEt from 10 : 1 to 5 : 1) to give diBoc **10** as white needles (11.5 g, 96%): mp 83.0-84.0 °C (from Et_2O-hexane); *R*f 0.50 (hexane/AcOEt, 2 : 1); FTIR (KBr) ν 1690, 1454, 1368, 1169, 1069, 737; ^1H NMR ($CDCl_3$) δ 1.45 (18H, s), 1.4-1.9 (8H, m), 3.47 (8H, m), 4.48 (4H, s), 7.30 (10H, s); ^{13}C NMR ($CDCl_3$) δ 27.24 (× 2), 28.52 (× 8), 60.47 (× 2, m), 69.96 (× 2), 72.79 (× 2), 80.0 (× 2, m), 127.37 (× 2), 127.46 (× 4), 128.19 (× 2), 138.38 (× 2), 152.0 (× 2, m). Calcd for $C_{32}H_{48}N_2O_6$ C, 69.03; H, 8.69; N, 5.03, found C, 69.01; H, 8.90; N, 5.11.

The *R,R*-enantiomer: mp 83.0-84.0 °C; $[\alpha]^{25}_D$ +30.4 (*c* 1.00, $CHCl_3$)

(4*S*,5*S*)-4,5-Di(*tert*-butoxycarbonylamino)-1,8-octanediol (9).

A mixture of **8** (231 mg, 0.415 mmol) in abs EtOH (10 mL) containing 200 mg of Pd on activated carbon (wet, Degussa type E 101 NE/W) was stirred at rt under H_2 atmosphere. After completion of the reaction (4 h), the mixture was filtered through Celite and concd. The crude product was crystallized from ether to afford diol **9** (156 mg, 100%) as a white powder: mp 147.0-148.0 °C (from CH_2Cl_2-acetone); R_f 0.35 (AcOEt/ MeOH, 10 : 1); FTIR (KBr) ν 3281, 1717, 1368, 1165, 1071; ^{1}H NMR ($CDCl_3$) δ 1.49 (18H, s), 1.4-1.9 (8H, m), 2.38 (2H, br), 3.69 (6H, m). Calcd for $C_{18}H_{36}N_2O_6$ C, 57.42; H, 9.64; N, 7.44, found C, 57.32; H, 9.71; N, 7.54.

The *R,R* enantiomer: mp 147.0-148.0 °C; $[\alpha]^{24}_D$ +50.3 (*c* 0.31, $CHCl_3$).

(*S,S*)-1,1'-Bis(*tert*-butoxycarbonyl)-2,2'-bipyrrolidine (10).

To a stirred solution of diol **11** (100 mg, 0.266 mmol) and Et_3N (295 μL, 2.12 mmol) in CH_2Cl_2 (5.4 mL) at 0 °C was added MsCl (151 mg, 1.32 mmol) and the mixture was stirred at rt for 10 min. The mixture was diluted with CH_2CH_2, washed with 5% aq $CuSO_4$, water, satd $NaHCO_3$, and satd NaCl, and dried (K_2CO_3). Evaporation of the solvent provided a crude dimesylate.

A solution of NaH (60% dispersion in oil, 76 mg, 1.98 mmol, washed with ether three times) in DMF (2.8 mL) was cooled to 0°C and the above-obtained dimesylate in DMF (5.7 mL) was added dropwise. The ice bath was removed and stirring was continued for 1.5 h. The mixture was quenched with aq NH_4Cl and filtered through Celite. The filtrate was concd and the residue was purified by silica gel column chromatography (hexane/AcOEt from 2 : 1 to 1 : 1) to afford diBoc **12** as a colorless oil (90 mg 100%): R_f 0.50 (hexane/AcOEt, 1 : 2); FTIR (neat) ν 1696, 1480, 1454, 1402, 1366, 1171, 1109; ^{1}H NMR ($CDCl_3$) δ 1.45 (18H, s), 1.6-2.1 (8H, m), 3.36 (4H, br), 3.83 (2H, br); MS *m/z* (rel intensity) 340 (7, M^+), 240 (7), 184 (2), 170 (14), 167 (17), 114 (100), 70 (79), 57 (45), 41 (8). HRMS calcd for $C_{18}H_{32}N_2O_4$ 340.2362, found 340.2375.

The *R,R*-enantiomer: $[\alpha]^{24}_D$ +40.6 (*c* 0.36, $CHCl_3$).

(*S,S*)-2,2'-Bipyrrolidine (11).

To a solution of diBoc **10** (384 mg, 1.13 mmol) in CH_2Cl_2 (1 mL) at 0 °C was added dropwise CF_3COOH (0.78 mL, 10.1 mmol) and the mixture was stirred at rt for 3 h. After completion of the reaction, the mixture was concd in vacuo at 0 °C and diluted with CH_2Cl_2. Under vigorous stirring at 0 °C, a few portions of 10 M aq NaOH were added and basified to pH 11 with NaOH pellets. The organic layer was separated and the aqueous layer was extracted carefully with CH_2Cl_2. The combined extracts were dried (K_2CO_3) and concd at 0 °C. The residure was purified by column chromatography (MeOH/CH_2Cl_2/25% aq NH_3, 17 : 2 : 1). The eluted product was concd at 0 °C and the residue was dissolved in CH_2Cl_2 and dried (K_2CO_3). Evaporation of the solvent at 0 °C gave pure **11** (151 mg, 95%) as a colorless oil: bp 70 °C/21 mmHg (Kugel-Rohr); R_f 0.12 (MeOH/CH_2Cl_2/25% aq NH_3, 17 : 2 : 1); FTIR (neat) ν 3285, 1557, 1400, 1073, 903; ^{1}H NMR ($CDCl_3$) δ 1.2-2.3 (8H, m), 2.6-3.3 (m, 6H), 4.00 (2H, br s); ^{13}C NMR ($CDCl_3$) δ 25.50 (× 2), 29.25 (× 2), 46.39 (× 2), 63.68 (× 2); MS *m/z* (rel intensity) 141 (59, M^+ + 1), 124 (18), 111 (17), 96 (2), 83 (4), 70 (100), 43 (3). HRMS calcd for $C_8H_{16}N_2$ + H 141.1392, found 141.1414.

(*S,S*)-1,1'-Dibenzoyl-2,2'-bipyrrolidine (12).

To a solution of **11** (68 mg, 0.486 mmol) and Et_3N (0.27 mL, 1.94 mmol) in CH_2Cl_2 (1 mL) at 0 °C was added a solution of benzoyl chloride (170 mg, 1.21 mmol) in CH_2Cl_2 (0.2 mL) and the mixture was stirred at 0 °C for 1 h. After quenching with aq NH_4Cl, the mixture was extracted with AcOEt. The combined extracts were washed with satd $NaHCO_3$ and satd NaCl, dried ($MgSO_4$), and concd. The crude product was purified by silica gel column chromatography (CH_2Cl_2/acetone, 9 : 1) to give dibenzoyl amide **12** (150 mg, 89%) as colorless plates: mp 148.0-149.0 °C; R_f 0.52 (CH_2Cl_2/acetone, 4 : 1); FTIR (KBr) ν 1618, 1576, 1424, 793, 723, 702; ^1H NMR ($CDCl_3$) δ 1.5-2.5 (8H, m), 2.9-3.4 (2H, m), 3.5-4.0 (2H, m), 4.56 (2H, br s), 7.0-7.6 (10H, m); ^{13}C NMR ($CDCl_3$) δ 24.22 (× 2), 28.28 (× 2), 49.16 (× 2), 58.89 (× 2), 127.09 (× 4), 128.07 (× 4), 129.41 (× 2), 137.19 (× 2), 170.73 (× 2). Calcd for $C_{22}H_{24}N_2O_2$ C, 75.83; H, 6.94; N, 8.04, found C, 75.66; H, 7.01; N, 7.98.

The *R,R*-enantiomer **13**: mp 160.5-161.5 °C; $[\alpha]^{24}_D$ +191.1 (*c* 0.51, $CHCl_3$).

The enantiomeric purity of **12** and **13** was confirmed by a Hitachi L-6200 HPLC using a DAICEL Chiralcel OD column eluted with hexane/2-propanol = 10 : 1 (flow rate 1 mL/min): t_R 61.26 min for **12** and 26.02 min for **13**, respectively.

X-Ray Crystal-Structure Determination: A colorless prismatic crystal of (*R,R*)-1,1'-dibenzoyl-2,2'-bipyrrolidine (**13**) with approximate dimensions of 0.35 × 0.20 × 0.05 mm was mounted on a glass fiber. All measurements were made on a Rigaku AFC7R diffractometer with graphite monochromated Cu-Kα radiation and a 12kW rotating anode generator. The structure was solved by direct methods (SHELXS86)[18] and refined through full-matrix least-squares calculations, anisotropically for non-hydrogen atoms and isotropically for hydrogen atoms, to a final R = 3.6% and R_W = 5.2%. Crystal data: $C_{22}H_{24}N_2O_2$, M = 348.44. Crystal system: orthorhombic. Space group: $P2_12_12_1$ (#19). Lattice parameters: a = 10.871(2) Å, b = 16.421 (1) Å, c = 10.649(2) Å. V = 1900.9(4) $Å^3$. Z = 4. F_{000} = 744.00. D_{calc} = 1.217 g/cm^3. Measured reflections: 1654. Observed reflections: 1234. μ(CuKα) = 6.21 cm^{-1}. For the molecular drawing, ORTEP program[19] was used.

Full structural details have been deposited with the Cambridge Crystallographic Center.

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