

Supporting Information

Asymmetric Desymmetrization of 2,2',6,6'-Tetrahydroxybiphenyl through Annulation with Enantiomerically Pure Bis(mesylate)

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General. Unless otherwise noted, ^1H and ^{13}C NMR spectra were recorded in CDCl_3 at 500 MHz and 125.8 MHz, respectively. All commercially available reagents were used without further purification unless otherwise noted. DMF, triethylamine, and pyridine were distilled from CaH_2 . THF was distilled from sodium benzophenone ketyl. Commercial anhydrous ZnCl_2 was dried over P_2O_5 in *vacuo* at 100 °C for 10 h. All reactions were performed under nitrogen or argon atmosphere. Organic extracts were dried over Na_2SO_4 . Flash chromatography was conducted on silica gel (Wakogel C-300). The ee values of 2,2'-biphenyldiols were established by HPLC analyses using a Chiracel AD column with 90:10:0.09 hexane:2-propanol:acetic acid as a mobile phase at a flow rate of 1 mL/min.

(S)-Methylethylene Bis(methanesulfonate) ((S)-7). To a solution of (S)-1,2-propane diols 1.52 g (20.0 mmol) and Et_3N (7.3 mL, 52.0 mmol) in CH_2Cl_2 (120 mL) at 0 °C was added slowly methanesulfonyl chloride (3.7 mL, 48.0 mmol) during 30 min. After being stirred at 0 °C for 1 h, the mixture was diluted with ether (50 mL) and hexane (50 mL), poured into water, and extracted twice with the solvents. The dried organic layers were concentrated in *vacuo*. The residue was purified by recrystallization from ethyl acetate and hexane to give 3.98 g (86 %) of (S)-7: mp 68-69 °C (recrystallized from ethyl acetate and hexane); ^1H NMR δ 1.50 (3H, d, $J = 6.6$ Hz), 3.11 (3H, s), 3.11 (3H, s), 4.27 (1H, dd, $J = 6.9$ and 11.5 Hz), 4.36 (1H, dd, $J = 3.0$ and 11.5 Hz), 5.04 (1H, d quintet, $J = 3.0$ and 6.6 Hz); ^{13}C NMR δ 17.42, 37.82, 38.69, 70.30, 75.56; FT-IR (KBr disk) 1355, 1342, 1182, 1177 cm^{-1} ; MS (CI) m/z (relative intensity) 233 (MH^+ , 100), 137 (70); HRMS (CI) calcd for $\text{C}_5\text{H}_{13}\text{O}_6\text{S}_2$: 233.0154, found 233.0143. Anal. Calcd for $\text{C}_5\text{H}_{13}\text{O}_6\text{S}_2$: C, 25.85; H, 5.21. Found: C, 25.96; H, 5.07.

Bis-Annulation Products 9 and 9': ^1H NMR δ 1.34 and 1.35 (6H, d, $J = 6.5$ Hz), 3.76 (2H, m), 4.27 (2H, m), 4.39 (2H, br d, $J = ca.$ 12 Hz), 7.00 (4H, m), 7.33-7.38 (2H, m); ^{13}C NMR δ 17.19 (for two isomers), 78.64 (for two isomers), 80.60 (for two isomers), 118.31, 118.39, 118.39, 118.47, 122.53, 122.64, 122.69, 129.80, 129.90, 130.01, 159.17, 159.20, 159.57, 159.47; FT-IR (KBr disk) 1224, 1054, 756, 723 cm^{-1} ; MS m/z (relative intensity) 298 (M^+ , 100), 149 (48); HRMS calcd for $\text{C}_{18}\text{H}_{18}\text{O}_4$: 298.1205, found 298.1197.

Bis(triflate) (aS,R)-10. To a solution of (aS,R)-8 (1.38 g, 5.34 mmol) in pyridine (10.7 mL) at 0 °C was added trifluoromethanesulfonic anhydride (2.7 mL, 16.02 mmol). After being stirred at rt for 10 h, the reaction mixture was diluted with ether, poured into aqueous 1N HCl, and extracted twice with ether. The dried organic layers were concentrated in *vacuo*. Purification of the residue by flash chromatography (10-40 % ethyl acetate in hexane) gave 2.46 g (88 %) of bis(triflate) (aS,R)-10:

mp 97-97.5 °C (recrystallized from benzene and hexane); $[\alpha]_D^{32}$ 97.8 (*c* 1.0, CHCl₃); ¹H NMR δ 1.38 (3H, d, *J* = 6.6 Hz), 3.78 (1H, dd, *J* = 10.6 and 12.2 Hz), 4.31 (1H, m), 4.46 (1H, dd, *J* = 3.2 and 12.2 Hz), 7.25 (4H, m), 7.54 (1H, t, *J* = 8.1 Hz), 7.56 (1H, t, *J* = 8.2 Hz); ¹³C NMR δ 17.04, 79.09, 81.68, 117.74 (2C), 118.31 (2C, q, *J* = 319 Hz), 120.46, 120.66, 122.76, 122.88, 131.37, 131.44, 146.98, 147.02, 160.51, 160.85; FT-IR (KBr disk) 1423, 1218, 798, 715 cm⁻¹; MS *m/z* (relative intensity) 522 (M⁺, 100), 240 (50), 95 (43); HRMS calcd for C₁₇H₁₂O₈F₆S₂: 521.9878, found 521.9874; Anal. Calcd for C₁₇H₁₂O₈F₆S₂: C, 39.09; H, 2.32. Found: C, 38.80; H, 2.29.

Diphenylation Product (a*S*,*R*)-11a. A solution of PhZnCl in THF was prepared by the reaction of ZnCl₂ (2.21 g, 16.22 mmol) and PhLi (0.85 M in cyclohexane-diethyl ether; 19.1 mL; 16.22 mmol) in THF (32 mL) at 0 °C for 15 min. To a mixture of (a*S*,*R*)-10 (1.57 g, 3.0 mmol) and PdCl₂(dppf) (0.12 g, 0.15 mmol) in THF (30 mL) at rt was added the resulting solution of PhZnCl (38.0 mL). After being stirred at 65 °C for 20 h, the reaction mixture was diluted with ether, poured into aq. NH₄Cl, and extracted twice with ether. The organic layers were washed with aqueous NaHCO₃, dried, and concentrated in *vacuo*. Purification of the residue by flash chromatography (20-60 % benzene in hexane) gave 1.08 g (95 %) of (a*S*,*R*)-11a: mp 215-216 °C (recrystallized from ethyl acetate and hexane); ¹H NMR δ 1.42, (3H, d, *J* = 6.5 Hz), 3.91 (1H, dd, *J* = 10.9 and 11.8 Hz), 4.44, (1H, m), 4.50 (1H, dd, *J* = 3.6 and 12.0 Hz), 6.42 (4H, m), 6.91 (2H, m), 6.95 (4H, m), 7.07 (2H, t, *J* = 7.6 Hz), 7.18-22 (2H, m), 7.33-7.38 (2H, m); ¹³C NMR δ 17.46, 79.73, 81.42, 120.85, 120.92, 125.96 (2C), 126.13, 126.16, 127.19, 127.21, 129.02, 129.09, 129.25, 129.28 (2C), 129.33, 140.50, 140.53, 142.88, 142.93, 160.07, 160.50; FT-IR (KBr disk) 1092, 1018, 758, 696 cm⁻¹; MS *m/z* (relative intensity) 378 (M⁺, 100), 321 (20), 69 (25); HRMS calcd for C₂₇H₂₂O₂: 378.1621, found 378.1611. Anal. Calcd for C₂₇H₂₂O₂: C, 85.69; H, 5.86. Found: C, 85.28; H, 5.90. The enantiomeric compound (a*R*,*S*)-11a was prepared from (a*R*,*S*)-10 in 84 % yield by a procedure similar to that described above.

Dibutylation Product (a*S*,*R*)-11b. The compound was prepared by a procedure similar to that described above. Purification by flash chromatography (3 % ethyl acetate in hexane) gave (a*S*,*R*)-11b (96%): ¹H NMR δ 0.73 (3H, t, *J* = 7.2 Hz), 0.75 (3H, t, *J* = 7.0 Hz), 1.10-1.19 (4H, m), 1.25-1.35 (5H, m, including d (3H, *J* = 6.6 Hz) at 1.30), 1.37-1.46 (2H, m), 2.44-2.53 (4H, m), 3.73 (1H, t, *J* = 11.2 Hz), 4.24 (1H, m), 4.34 (1H, dd, *J* = 3.2 and 12.0 Hz), 7.04 (2H, d, *J* = 7.8 Hz), 7.12 (2H, t, *J* = 7.2 Hz), 7.32 (1H, t, *J* = 7.8 Hz), 7.34 (1H, t, *J* = 8.2 Hz); ¹³C NMR δ 13.62, 13.63, 17.32 (2C), 22.09, 22.24, 32.93, 33.13, 33.30, 79.79, 81.38, 119.33, 119.44, 124.65 (2C), 128.80, 128.84, 129.91, 129.94, 142.43, 142.45, 159.36, 159.77; FT-IR (KBr disk) 1074, 1039, 760, 732 cm⁻¹; MS *m/z* (relative intensity) 338 (M⁺, 75), 295 (100), 253 (36); HRMS calcd for C₂₃H₃₀O₂: 338.2247, found 338.2236.

(*S*)-1,1':2',1'':2'',1'''-Quaterphenyl-3',5''-diol ((*S*)-12a).^{2e} To a solution of (a*S*,*R*)-11a (0.11 g, 0.3 mmol) in CH₂Cl₂ (3.0 mL) at 0 °C was added BBr₃ (0.5 mL, 5.4 mmol). After being stirred for 15 h at rt, the reaction mixture was diluted with CH₂Cl₂, poured into ice, and extracted twice with ether. The dried organic layers were concentrated in *vacuo*. Purification by flash chromatography (3% ethyl acetate in benzene) gave 0.09 g (91 %) of (*S*)-12a. $[\alpha]_D^{18}$ -147 (*c* 1.01,

EtOH); $[\alpha]_{\text{D}}^{21}$ -88.0 (*c* 1.0, CHCl₃); ee 99%. The enantiomeric compound (*R*)-**12a** was prepared from (*aR,S*)-**11a** in 91 % yield by a procedure similar to that described above. (*R*)-**17a**: $[\alpha]_{\text{D}}^{21}$ +88.4 (*c* 1.0, CHCl₃); ee 99 % .

(S)-6,6'-Dibutyl-2,2'-dihydroxybiphenyl ((S)-12b).^{2e} The compound was prepared by a procedure similar to that described above. Purification by flash chromatography (3-20 % ethyl acetate in hexane) gave (*S*)-**12b** (82 %): $[\alpha]_{\text{D}}^{22}$ -25.58 (*c* 0.43, EtOH); 97 % ee.

Annulation Product (aS,R)-13a. To a suspension of (*aS,R*)-**8** (0.050 g, 0.20 mmol) and K₂CO₃ (0.060 g, 0.46 mmol) in DMF (10 mL) at 80 °C was added a solution of 1,5-dibromopentane (0.03 mL, 0.2 mmol) in DMF (2 mL) during 5 h by using a syringe pump. After being stirred at this temperature for 16 h, the reaction mixture was poured into aqueous 1N HCl and extracted twice with benzene. The dried organic layers were concentrated in *vacuo*. Purification of the residue by flash chromatography (3-30 % ethyl acetate in hexane) gave 0.05 g (75%) yield of (*aS,R*)-**13a**: mp 137-139 °C (recrystallized form ethyl acetate and hexane); ¹H NMR δ 1.31 (3H, d, *J* = 6.3 Hz), 1.69 (2H, m), 1.78-1.89 (4H, m), 3.73 (1H, t, *J* = 11.8 Hz), 4.10-4.12 (2H, m), 4.23-4.28 (1H, m), 4.33-4.37 (3H, m), 6.80 (4H, m), 7.29 (2H, m); ¹³C NMR δ 17.26, 25.36, 26.29, 26.32, 67.58, 67.71, 78.96, 80.65, 107.84, 107.86, 114.45, 114.55, 118.09, 118.17, 129.06, 129.18, 156.86, 156.94, 159.92, 160.35; FT-IR (KBr disk) 1090, 796, 721 cm⁻¹; MS *m/z* (relative intensity) 326 (M⁺, 100), 229 (19); HRMS calcd for C₂₀H₂₂O₄: 326.1519, found 326.1510. Anal. Calcd for C₂₀H₂₂O₄: C, 73.59; H, 6.80. Found: C, 73.32; H, 6.75.

Annulation Product (aS,R)-13b. The compound was prepared from (*aS,R*)-**8** and 1,6-dibromohexane by a procedure similar to that described above. Purification by flash chromatography (5-30 % ethyl acetate in hexane) gave (*aS,R*)-**13b** (78 %): ¹H NMR δ 1.32 (3H, d, *J* = 6.5 Hz), 1.55-1.61 (4H, m), 1.74-1.78 (4H, m), 3.74 (1H, dd, *J* = 11.0 and 11.9 Hz), 4.00-4.05 (2H, m), 4.21-4.28 (3H, m), 4.35 (1H, dd, *J* = 3.4 and 12.2 Hz), 6.80 (2H, d, *J* = 8.9 Hz), 6.81 (2H, d, *J* = 8.2 Hz), 7.30-7.35 (2H, m); ¹³C NMR δ 17.20, 24.04, 24.08, 25.74, 25.76, 66.63 (2C), 79.13, 80.78, 106.72, 106.78, 113.98, 114.04, 117.49, 117.50, 129.13, 129.24, 156.92, 156.98, 159.97, 160.42; FT-IR (KBr disk) 1064, 791, 721 cm⁻¹; MS *m/z* (relative intensity) 340 (M⁺, 100), 229 (25); HRMS calcd for C₂₁H₂₄O₄: 340.1675, found 340.1660.

Biphenyldiol (S)-14a.^{2e} A solution LDBB in THF (0.17 M) was prepared by a reaction of Li (183 mg, 2.60 mmol) with 4,4'-di-*tert*-butylbiphenyl (0.80 g, 3.00 mmol) in THF (15 mL) at 0 °C for 14 h. To a reaction flask containing (*aS,R*)-**13a** (0.12 g, 0.38 mmol) at 0 °C was added the LDBB solution in THF (8.5 mL). After being stirred at 0 °C for 1 h, the reaction mixture was poured into aqueous 1N HCl and extracted twice with ether. The dried organic layers were concentrated in *vacuo*. Purification of the residue by flash chromatography (20-40% ethyl acetate in hexane) gave 0.10 g (88% yield) of (*S*)-**14a**: $[\alpha]_{\text{D}}^{23}$ +200 (*c* 0.5, THF); ee 99% .

Biphenyldiol (S)-14b.^{2e} The compound was prepared from (*aS,R*)-**13b** in 97 % yield by a procedure similar to that described above. (*S*)-**14b**: $[\alpha]_{\text{D}}^{22}$ +125 (*c* 0.45, EtOH); ee 97 % .