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Supporting Information

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Non-C_2-Symmetric, Chirally Economical, and Readily Tunable Linked-BINOLs: Design and Application in Direct Catalytic Asymmetric Mannich-type Reaction

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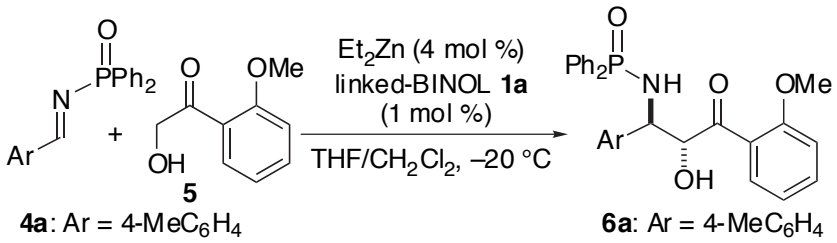
Experimental Section

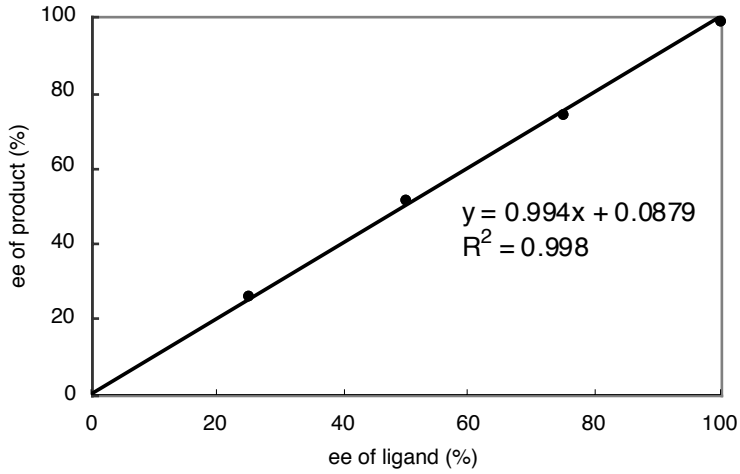
General: Infrared (IR) spectra were recorded on a JASCO FT/IR 410 Fourier transform infrared spectrophotometer. NMR spectra were recorded on a JEOL JNM-LA500 spectrometer, operating at 500 MHz for ^{1}H NMR and 125.65 MHz for ^{13}C NMR. Chemical shifts in $CDCl_3$ were reported downfield from TMS (= 0) or in the scale relative to $CHCl_3$ (7.24 ppm) for ^{1}H NMR. For ^{13}C NMR, chemical shifts were reported in the scale relative to $CHCl_3$ (77.0 ppm for ^{13}C NMR) as an internal reference. Optical rotations were measured on a JASCO P-1010 polarimeter. ESI mass spectra were measured on Waters-ZQ4000. Column chromatography was performed with silica gel Merck 60 (230–400 mesh ASTM). The enantiomeric excess (ee) was determined by HPLC analysis. HPLC was performed on JASCO HPLC systems consisting of the following: pump, PU-2080; detector, UV-2075, measured at 254 nm; column, DAICEL CHIRALCEL OD-H, CHIRALPAK AS-H; mobile phase, hexane–2-propanol; Reactions were carried out in dry solvents under an argon atmosphere, unless otherwise stated. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. Et_2Zn (1.0 M, in hexanes) was purchased from Aldrich and used as received. Dpp-imines **4** were prepared as described in lit. Jennings, W. B.; Lovely, C. J. *Tetrahedron* **1991**, *47*, 5561. Other reagents were purified by the usual methods.

Linked-BINOL **1a** is commercially available from Wako Pure Chemical Industries, Ltd. Cat. No. 152-02431 for (*S*,*S*)-ligand, No. 155-02421 for (*R*,*R*)-ligand. Fax +1-804-271-7791 (USA), +81-6-6201-5964 (Japan), +81-3-5201-6590 (Japan).

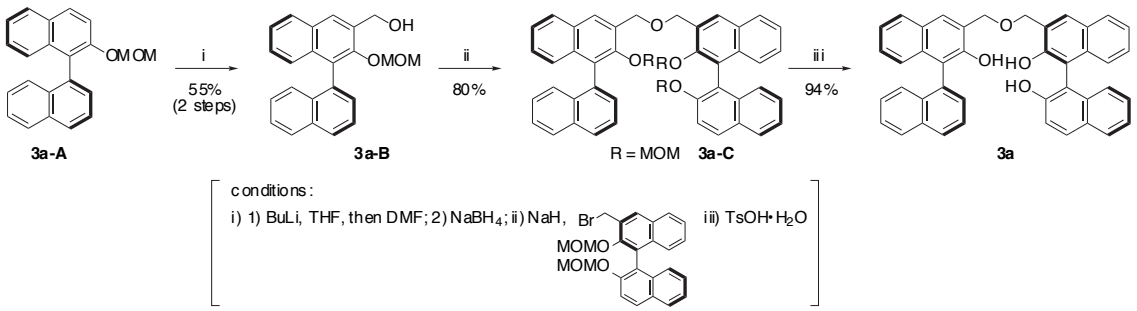
<Relationship between Ee of Mannich-adduct and Ligand>(Figure 2)

There was linear relationship between ee of Mannich-adduct **6a** from Dpp-imine **4a** and ee of linked-BINOL, as summarized in the Figure below. Reaction rate was almost same in all cases using ligand of >99% ee, 75% ee, 50% ee, 25% ee, and 0% ee. Enantiomeric excess is shown as average of two runs.



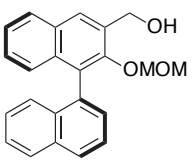


Ligand Synthesis (Figure 3):

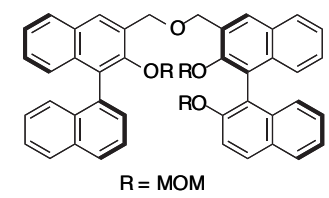


(*S*)-3-Hydroxymethyl-2-methoxymethyloxy-1,1'-binaphthalene: To a stirred solution of compound **3a-A** (1100 mg, 3.5 mmol) in THF (25 mL) at –78 ℃ was added BuLi (1.58 M in hexane, 5.6 mL, 8.75 mmol). After stirring at –78 ℃ for 3 h, DMF (1.35 mL, 17.5 mmol) was added. The mixture was gradually warmed to room temperature over 2 h, and then was quenched with *sat. aq.* NH_4Cl. The mixture was extracted with ethyl acetate (x 3). Organic layers were washed with brine, dried over Na_2SO_4, and evaporated to give aldehyde as a crude material. The crude aldehyde was dissolved in THF (12 mL)/MeOH (5 mL), and the solution was cooled at 0 °C. $NaBH_4$ (160 mg, 3.5 mmol) was added, and the reaction mixture was stirred at room temperature. The reaction mixture was quenched with H_2O, extracted with diethyl ether (x 3). The organic layers were washed with brine, dried over Na_2SO_4 and $MgSO_4$. After evaporation, the residue was purified by

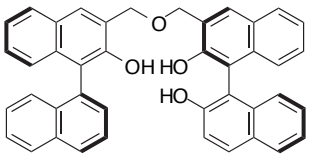
silica gel flash column chromatography (hexane/ethyl acetate = 10/1 to 2/1) to give alcohol **3a-B** (662 mg, 55%) as colorless viscous oil; IR (KBr) ν 3485, 3044, 2926 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.18 (s, 3H), 3.49 (brs, 1H), 4.42 (d, *J* = 6.3 Hz, 1H), 4.51 (d, *J* = 6.3 Hz, 1H), 4.91 (s, 2H), 7.10-7.70 (m, 8H), 7.85-8.05 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 57.0, 62.0, 99.5, 125.2, 125.4, 125.9, 126.0, 126.1, 126.3, 126.4, 127.9, 128.3, 128.9, 129.1, 129.1, 130.9, 132.7, 133.6, 133.8, 133.8, 134.2, 152.5; ESI-MS *m/z* 367 $[M+Na]^+$; HRMS (FAB): *m/z* calcd for $C_{23}H_{20}O_3$ $[M]^+$: 344.1412; found: 344.1417.



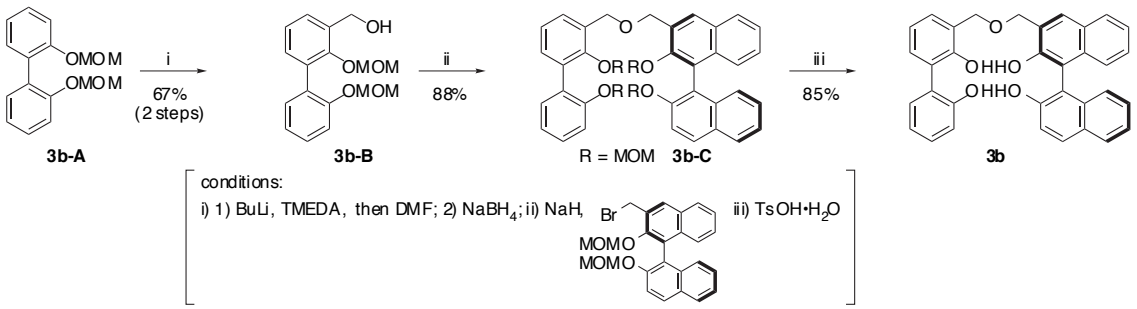
(*S*)-2,2'-Bis(methoxymethyloxy)-3-[(*S*)-2-methoxymethyloxy-1,1'-binaphthalen-3-ylmethoxymethyl]-1,1'-binaphthalene : To a solution of alcohol **3a-B** (603 mg, 1.75 mmol) in DMF (15 mL) at 0 ℃ was added NaH (60% purity, 105 mg, 2.6 mmol). The mixture was stirred at 0 ℃ for 30 min, then (*S*)-bromomethyl-MOM-BINOL (981 mg, 2.1 mmol) was added. After stirring at room temperature over night, the mixture was quenched with *sat. aq.* NH_4Cl, and extracted with diethyl ether (x 3). The organic layers were washed with H_2O, brine, and dried over Na_2SO_4 and $MgSO_4$. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 10/1 to 5/1) to give **3a-C** (1.02 g, y. 80%) as colorless foam; IR (KBr) ν 3057, 2952, 1154 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.80 (s, 3H), 2.87 (s, 3H), 3.16 (s, 3H), 4.57 (d, *J* = 5.4 Hz, 1H), 4.59 (d, *J* = 5.4 Hz, 1H), 4.60 (d, *J* = 5.5 Hz, 1H), 4.69 (d, *J* = 5.5 Hz, 1H), 5.02 (d, *J* = 7.0 Hz, 1H), 5.09 (s, 2H), 5.10 (s, 2H), 5.13 (d, *J* = 7.0 Hz, 1H), 7.15-7.65 (m, 15H), 7.80-8.00 (m, 6H) 8.20 (s, 1H), 8.21 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 55.9, 56.6, 56.6, 68.7, 68.7, 94.8, 99.3, 99.5, 116.5, 120.7, 124.1, 125.0, 125.1, 125.3, 125.4, 125.6, 125.7, 125.9, 126.0, 126.0, 126.1, 126.2, 126.3, 126.7, 127.8, 127.9, 128.0, 128.1, 128.2, 128.4, 128.6, 129.1, 129.6, 129.8, 130.8, 130.9, 131.8, 131.8, 133.0, 133.5, 133.6, 133.7, 134.0, 134.1, 151.3, 151.9, 152.9; ESI-MS *m/z* 753 $[M+Na]^+$; HRMS (FAB): *m/z* calcd for $C_{48}H_{42}O_7$ $[M]^+$: 730.2931; found: 730.2941.

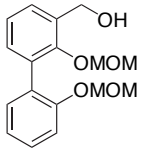


3-[(*S*)-2-Hydroxy-1,1'-binaphthalen-3-ylmethoxymethyl]-(*S*)-1,1'-bi-2-naphthol (3a): A mixture of **3a-C** (950 mg, 1.3 mmol) and $TsOH•H_2O$ (49 mg, 0.26 mmol) in CH_2Cl_2 (15 mL)/MeOH (15 mL) was stirred at 40 ℃. After 24 h, *sat. aq.* $NaHCO_3$ was added, and the mixture was extracted with ethyl acetate (x 3). The organic layers were washed with brine, and dried over Na_2SO_4. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 5/1 to 4/1) to give **3a** (728 mg, y. 94%) as colorless foam; IR (KBr) ν 3511, 3384, 3056, 1108, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.00 (d, *J* = 13 Hz, 1H), 5.01 (s, 2H), 5.03 (d, *J* = 13 Hz, 1H), 5.03 (s, 1H), 6.08 (s, 1H), 6.56 (s, 1H), 7.05-7.60 (m, 15H), 7.75-8.00 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 70.4, 70.5, 112.4, 112.5, 117.6, 120.0,



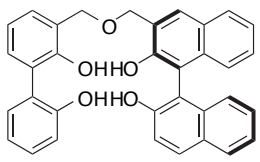
123.6, 124.1, 124.3, 124.4, 124.9, 125.0, 125.5, 125.8, 126.2, 126.6, 127.0, 127.3, 127.9, 128.2, 128.2, 128.3, 128.4, 128.8, 128.9, 129.2, 129.3, 129.8, 130.7, 132.0, 132.6, 133.4, 133.5, 133.9, 134.1, 150.1, 152.0, 152.0 ; ESI-MS *m/z* 621 $[M+Na]^+$; $[\alpha]_D^{24}$ –55.4 (*c* 1.01, $CHCl_3$); HRMS (FAB): *m/z* calcd for $C_{42}H_{30}O_4$ $[M]^+$: 598.2144; found: 598.2150.



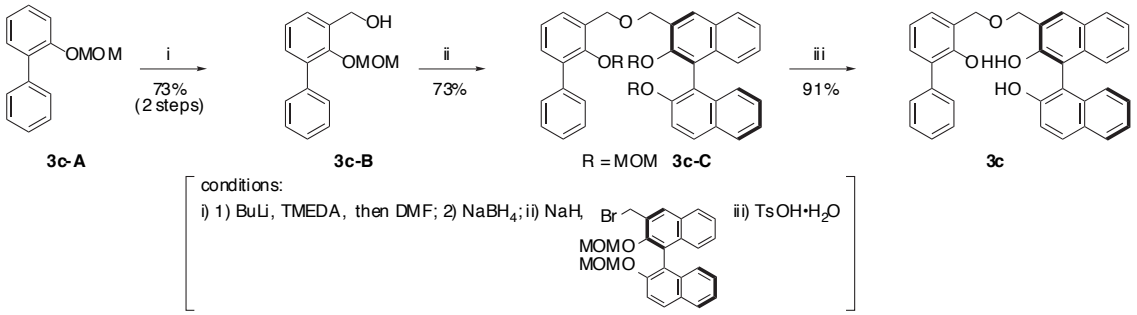


3-Hydroxymethyl-2,2'-bis(methoxymethyloxy)biphenyl: To a stirred solution of compound **3b-A** (5.94 g, 21.6 mmol) and TMEDA (3.8 mL, 26 mmol) in THF (80 mL) at –78 ℃ was added BuLi (1.56 M in hexane, 15 mL, 23.4 mmol). After stirring at 0 ℃ for 30 min, the mixture was cooled down to –78 ℃ again. Then, DMF (2.5 mL) was added, and the mixture was gradually warmed to 0 ℃. The mixture was quenched with *sat. aq.* NH_4Cl. The mixture was extracted with ethyl acetate. Organic layers were washed with brine, dried over $MgSO_4$, and evaporated to give aldehyde as a crude material. The crude aldehyde was dissolved in MeOH (60 mL), and the solution was cooled at 0 ℃. $NaBH_4$ (1.16 g, 25 mmol) was added, and the reaction mixture was stirred at 0 ℃. The reaction mixture was quenched with acetone and *sat. aq.* NH_4Cl, and was extracted with ethyl acetate. The organic layer was washed with brine and dried over $MgSO_4$. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 4/1 to 1/1) to give alcohol **3b-B** (4.38 g, y. 67%, 2 steps) as colorless solid; IR (KBr) ν 3482, 2929, 2936, 2906 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.28 (t, *J* = 6.5 Hz, 1H), 3.32 (s, 3H), 3.33 (s, 3H), 4.58 (s, 2H), 4.71 (d, *J* = 6.5 Hz, 2H), 5.09 (s, 2H), 4.51 (d, *J* = 6.3 Hz, 1H), 4.91 (s, 2H), 7.05-7.38 (m, 7H); ^{13}C NMR ($CDCl_3$) δ 55.9, 57.0, 94.8, 99.2, 115.4, 121.9, 124.3, 128.6, 129.0, 129.2, 131.4, 131.7, 132.1, 134.6, 154.0, 154.4; ESI-MS *m/z* 327 $[M+Na]^+$; HRMS (FAB): *m/z* calcd for $C_{17}H_{20}O_5$ $[M]^+$: 304.1311; found: 304.1308.

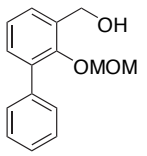
3-(2,2'-Dihydroxy-biphenyl-3-ylmethoxymethyl)-(*S*)-1,1'-bi-2-naphthol: To a solution of alcohol **3b-B** (913 mg, 3 mmol) in THF (5 mL)/DMF (3 mL) at 0 ℃ was added NaH (60% purity, 150 mg, 3.75 mmol). The mixture was stirred at 0 ℃ for 30 min, then (*S*)-bromomethyl-MOM-BINOL (1.40 g, 3 mmol) was added. After stirring at room temperature over night, the mixture was quenched with *sat. aq.* NH_4Cl, and extracted with diethyl ether (x 3). The organic layers were



washed with H_2O, brine, and dried over $MgSO_4$. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 4/1 to 2/1) to give **3b-C** (1.82 g, y. 88%). A mixture of **3b-C** (1.82 g, 2.63 mmol) and TsOH•H_2O (200 mg) in CH_2Cl_2 (4 mL)/MeOH (4 mL) was stirred at 38 ℃. After 12 h, *sat. aq.* $NaHCO_3$ was added, and the mixture was extracted with ethyl acetate (x 3). The organic layers were washed with brine, and dried over $MgSO_4$. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 4/1 to 3/1) to give **3b** (1.15 g, y. 85%) as colorless powder; IR (KBr) ν 3480, 3291, 3057, 1210, 752 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.91 (d, *J* = 11 Hz, 1H), 4.91 (s, 2H), 4.96 (d, *J* = 11 Hz, 1H), 5.17 (s, 1H), 5.85 (s, 1H), 6.51 (s, 1H), 6.90-7.40 (m, 14H), 7.80-8.00 (m, 4H), 8.26 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 70.0, 71.7, 111.0, 112.3, 117.6, 117.8, 121.0, 121.2, 122.9, 123.9, 124.1, 124.3, 124.4, 124.9, 125.6, 126.0, 127.4, 127.6, 128.3, 128.4, 128.9, 129.3, 129.3, 130.7, 131.2, 131.3, 132.2, 133.3, 133.5, 151.3, 152.1, 152.5, 153.4 ; ESI-MS *m/z* 537 $[M+Na]^+$; $[\alpha]_D^{24}$ –40.4 (*c* 1.05, $CHCl_3$); HRMS (FAB): *m/z* calcd for $C_{34}H_{26}O_5$ $[M]^+$: 514.1780; found: 514.1772.



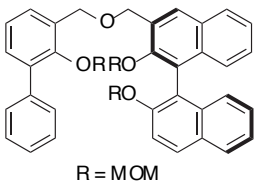
3-Hydroxymethyl-2-(methoxymethyloxy)biphenyl:



To a stirred solution of compound **3c-A** (6.43 g, 30 mmol) and TMEDA (11.3 mL, 75 mmol) in THF (150 mL) at –78 ℃ was added BuLi (1.60 M in hexane, 46.9 mL, 75 mmol). After stirring at 0 ℃ for 45 min, the mixture was cooled down to –78 ℃ again. DMF (11.6 mL, 150 mmol) was added and the mixture was stirred at –78 ℃ for 30 min. Then, the mixture was quenched with *sat. aq.* NH_4Cl. The mixture was extracted with ethyl acetate (x 3). Organic layers were washed with brine, dried over Na_2SO_4, and evaporated to give aldehyde as a crude material. The crude aldehyde was dissolved in THF (90 mL)/MeOH (35 mL), and the solution was cooled at 0 ℃. $NaBH_4$ (1.7 g, 45 mmol) was added, and the reaction mixture was stirred at 0 ℃ for 45 min. The reaction mixture was quenched with H_2O, extracted with diethyl ether (x 3). The organic layers were washed with brine, dried over Na_2SO_4 and $MgSO_4$. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 4/1 to 2/1) to give alcohol **3c-B** (5.35 g, y. 73%) as colorless viscous oil; IR (neat) ν 3420, 3060, 2938, 1157 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.34 (t, *J* = 6.3 Hz, 1H), 3.35 (s, 3H), 4.55 (s, 2H), 4.72 (d, *J* = 6.3 Hz, 2H), 7.19 (dd,

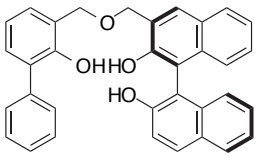
J = 8.0 Hz, 1H), 7.25-7.45 (m, 5H), 7.45-7.55 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 57.2, 61.1, 99.3, 124.9, 127.2, 128.4, 129.1, 129.2, 131.0, 134.8, 135.1, 138.4, 153.4; ESI-MS m/z 267 $[M+Na]^+$; HRMS (FAB): m/z calcd for $C_{15}H_{16}O_3$ $[M]^+$: 244.1099; found: 244.1106.

(*S*)-2,2'-Bis(methoxymethyloxy)-3-[2-(methoxymethyloxy)biphenyl-3-ylmethoxymethyl]-1,1'-binaphthalene:

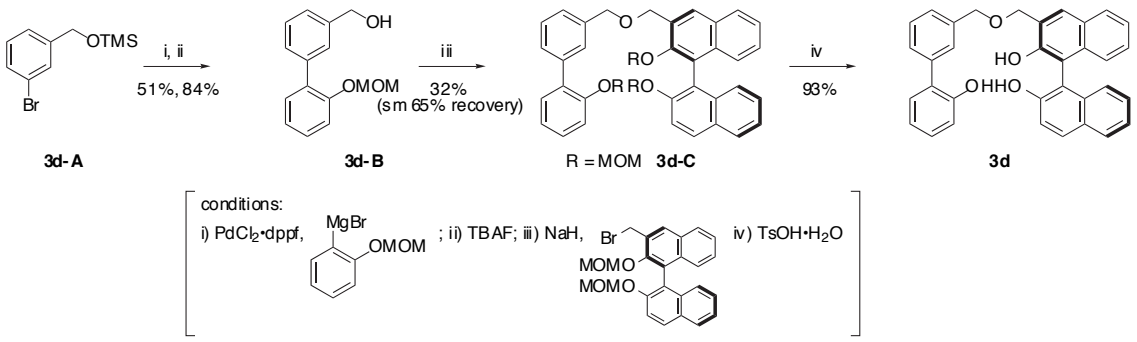


To a solution of alcohol **3c-B** (733 mg, 3 mmol) in DMF (30 mL) at 0 ℃ was added NaH (60% purity, 86 mg, 3.6 mmol). The mixture was stirred at 0 ℃ for 30 min, then (*S*)-bromomethyl-MOM-BINOL (1.40 g, 3 mmol) was added. After stirring at room temperature for 24 h, the mixture was quenched with *sat. aq*. NH_4Cl, extracted with diethyl ether (x 3). The organic layers were washed with H_2O, brine, and dried over Na_2SO_4 and $MgSO_4$. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 10/1) to give **3c-C** (1.38 g, y. 73%) as colorless viscous oil; IR (KBr) ν 3059, 2932, 1154 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.86 (s, 3H), 3.15 (s, 3H), 3.17 (s, 3H), 4.58 (d, J = 5.5 Hz, 1H), 4.63 (s, 2H), 4.66 (d, J = 5.5 Hz, 1H), 4.92 (s, 2H), 5.00 (s, 2H), 5.01 (d, J = 7.0 Hz, 1H), 5.11 (d, J = 7.0 Hz, 1H), 7.10-8.05 (m, 18H), 8.15 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 55.9, 56.5, 57.2, 68.1, 68.5, 94.9, 99.3, 99.7, 116.5, 120.8, 124.1, 124.6, 124.9, 125.3, 125.6, 125.7, 126.0, 126.7, 127.1, 127.8, 128.0, 128.3, 128.3, 128.8, 129.4, 129.6, 129.8, 130.6, 130.9, 131.9, 132.4, 132.4, 134.0, 135.3, 138.8, 151.8, 152.6, 152.9; ESI-MS m/z 653 $[M+Na]^+$; HRMS (FAB): m/z calcd for $C_{40}H_{38}O_7$ $[M]^+$: 630.2618; found: 630.2611.

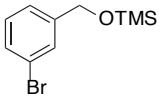
(*S*)-3-(2-Hydroxy-biphenyl-3-ylmethoxymethyl)-1,1'-bi-2-naphthol:



A mixture of **3c-C** (1.10 g, 1.75 mmol) and TsOH•H_2O (66 mg, 0.35 mmol) in CH_2Cl_2 (15 mL)/MeOH (15 mL) was stirred at 40 ℃. After 20 h, *sat. aq*. $NaHCO_3$ was added, and the mixture was extracted with ethyl acetate (x 3). The organic layers were washed with brine, and dried over Na_2SO_4. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 5/1 to 2/1) to give **3c** (0.794 g, y. 91%) as colorless foam; IR (KBr) ν 3510, 3392, 3057, 1213, 756 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.86 (s, 2H), 4.92 (d, J = 13 Hz, 1H), 4.95 (d, J = 13 Hz, 1H), 5.07 (s, 1H), 6.11 (s, 1H), 6.93 (dd, J = 7.5, 7.7 Hz, 1H), 7.07 (s, 1H), 7.10-7.50 (m, 14H), 7.80-7.95 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 69.8, 71.2, 111.6, 112.1, 117.7, 120.1, 122.9, 123.8, 124.3, 124.3, 125.4, 127.2, 127.3, 127.5, 128.3, 128.3,128.5, 128.8, 129.1, 129.3, 129.3, 130.2, 130.8, 131.0, 133.3, 133.4, 137.5, 151.6, 152.3, 152.5; ESI-MS m/z 521 $[M+Na]^+$; $[\alpha]_D^{25}$ –51.2 (c 0.98, $CHCl_3$); HRMS (FAB): m/z calcd for $C_{34}H_{26}O_4$ $[M]^+$: 498.1831; found: 498.1838.

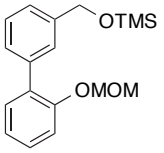


1-Bromo-3-(trimethylsilyloxy)methyl-benzene:



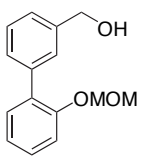
To a mixture of *m*-Br-benzyl alcohol (7.48 g, 40 mmol) and Et_3N (8.4 mL, 60 mmol) in THF (60 mL) at 0 ℃ was added TMSCl (6.52 g, 60 mmol). The mixture was stirred at room temperature for 1 h, then was poured onto ice cooled *sat. aq*. $NaHCO_3$. The mixture was extracted with diethyl ether (x 3). The organic layers were washed with H_2O, brine, and dried over Na_2SO_4 and $MgSO_4$. After evaporation, the residue was purified by silica gel flash column chromatography to give TMS-ether **3d-A** (8.21 g, y. 79%) as colorless oil; IR (neat) ν 2956, 1256, 1104 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.16 (s, 9H), 4.65 (s, 2H), 7.10-7.40 (m, 3H), 7.48 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 0.48, 63.7, 122.4, 124.8, 129.4, 129.8, 130.0, 143.3; ESI-MS *m/z* 367 $[M+Ag]^+$.

2-Methoxymethyloxy-3'-(trimethylsilyloxy)methyl-biphenyl:



To a mixture of $PdCl_2$•dppf (45.7 mg, 0.0625 mmol) and **3d-A** (6.48 g, 25 mmol) in THF (40 mL) at room teperature was added Grignard reagent prepared from MOM-protected -*o*-Br-phenol (5.97 g, 27.5 mmol) and Mg (1.00 g, 41.25 mmmol) in THF (35 mL). The mixture was stirred at 50 ℃ for 23 h, then MeOH (10 mL) was added. The mixture was filtered through Celite pad, and the solvent was evaporated. The residue was purified by silica gel flash column chromatography (hexane/ethyl acetate =1/0 to 10/1) to give biphenyl TMS-ether (4.07 g, y. 51%) as colorless oil; IR (neat) ν 2955, 1250, 1079 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.16 (s, 9H), 3.38 (s, 3H), 4.74 (s, 2H), 5.10 (s, 2H), 7.07 (ddd, *J* = 1.2, 7.6, 7.6 Hz, 1H), 7.15-7.45 (m, 6H), 7.49 (s,1H); ^{13}C NMR ($CDCl_3$) δ -0.39, 56.0, 64.7, 94.9, 115.5, 122.2, 125.2, 127.7, 127.9, 128.3, 128.5, 130.9, 131.8, 138.5, 140.5, 154.1; ESI-MS *m/z* 339 $[M+Na]^+$; HRMS (FAB): *m/z* calcd for $C_{18}H_{24}O_3Si$ $[M]^+$: 316.1495; found: 316.1485.

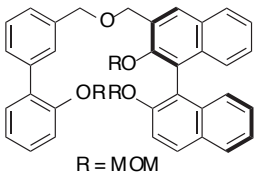
3'-Hydroxymethyl-2-methoxymethyloxy-biphenyl:



To a solution of biphenyl TMS-ether (3.48 g, 11 mmol) in THF (50 mL) at room temperature was added TBAF (15.4 mL, in THF, 1 M, 15.4 mmol). The mixture was stirred at room temperature for 20 min, and H_2O was added. The mixture was extracted with diethyl ether (x 3). The organic layers were washed with H_2O, brine and was dried over Na_2SO_4 and $MgSO_4$. After evaporation, the residue was purified by silica gel flash column choromatography (hexane/ethyl acetate =

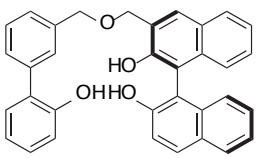
4/1) to give **3d-B** (2.26 g, y. 84%) as colorless viscous oil; IR (neat) ν 3390, 2933 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.41 (brs, 1H), 3.35 (s, 3H), 4.67 (s, 2H), 5.07 (s, 2H), 6.95-7.55 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 56.0, 65.2, 94.8, 115.5, 122.2, 125.5, 128.0, 128.1, 128.6, 128.7, 130.9, 131.5, 138.7, 140.6, 154.0; ESI-MS *m/z* 267 $[M+Na]^+$; HRMS (FAB): *m/z* calcd for $C_{15}H_{16}O_3$ $[M]^+$: 244.1099; found: 244.1092.

(*S*)-2,2'-Bis(methoxymethyloxy)-3-[2'-(methoxymethyloxy)biphenyl-3-ylmethoxymethyl]-1,1'-binaphthalene:



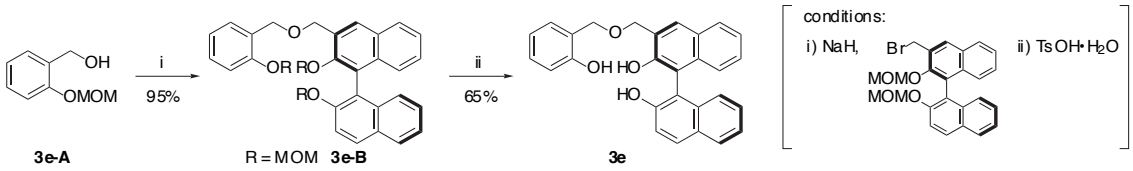
To a solution of alcohol **3d-B** (977 mg, 4 mmol) in DMF (40 mL) at 0 ℃ was added NaH (60% purity, 192 mg, 4.8 mmol). The mixture was stirred at 0 ℃ for 50 min, then (*S*)-bromomethyl-MOM-BINOL (2.80 g, 6 mmol) was added. After stirring at room temperature for 24 h, the mixture was quenched with H_2O, and extracted with diethyl ether (x 3). The organic layers were washed with H_2O, brine, and dried over Na_2SO_4 and$MgSO_4$. After evaporation, the residue was purified by silica gel flash column choromatography (hexane/ethyl acetate = 10/1 to 5/1) to give **3d-C** (795 mg, y. 32%, 65% of **3d-B** was recovered) as colorless viscous oil; IR (neat) ν 3060, 2953, 1152 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.80 (s, 3H), 3.10 (s, 3H), 3.32 (s, 3H), 4.55 (d, *J* = 5.8 Hz, 1H), 4.64 (d, *J* = 5.8 Hz, 1H), 4.80 (s, 2H), 4.95 (s, 2H), 4.97 (d, *J* = 7.5 Hz, 1H), 5.07 (s, 2H), 5.07 (d, *J* = 7.5 Hz, 1H), 6.95-7.70 (m, 15H), 7.75-7.95 (m, 3H), 8.12 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 55.7, 55.9, 56.3, 68.1, 72.8, 94.6, 94.8, 99.1, 115.4, 116.3, 120.5, 122.1, 124.0, 124.9, 125.2, 125.4, 125.5, 125.9, 126.4, 126.6, 127.7, 127.8, 128.0, 128.2, 128.5, 128.8, 128.9, 129.5, 129.7, 130.8, 130.8, 131.5, 131.7, 133.3, 133.8, 137.9, 138.6, 151.7, 152.7, 154.0; ESI-MS *m/z* 653 $[M+Na]^+$; HRMS (FAB): *m/z* calcd for $C_{40}H_{38}O_7$ $[M]^+$: 630.2618; found: 630.2611.

(*S*)-3-(2'-Hydroxy-biphenyl-3-ylmethoxymethyl)-1,1'-bi-2-naphthol:

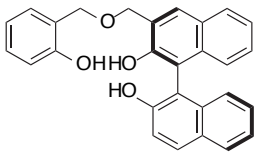


A mixture of **3d-C** (794 mg, 1.26 mmol) and TsOH•H_2O (48 mg, 0.25 mmol) in CH_2Cl_2 (15 mL)/MeOH (15 mL) was stirred at 40 ℃. After 28 h, *sat. aq.* $NaHCO_3$ was added, and the mixture was extracted with ethyl acetate (x 3). The organic layers were washed with brine, and dried over Na_2SO_4. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 5/1 to 2/1) to give **3c** (582 mg, y. 93%) as colorless foam; IR (KBr) ν 3511, 3421, 752 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.73 (s, 2H), 4.91 (d, *J* = 13 Hz, 1H), 4.94 (d, *J* = 13 Hz, 1H), 5.23 (brs, 2H), 6.30 (brs, 1H), 6.85-7.00 (m, 2H), 7.05-7.55 (m, 13H), 7.80-7.95 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 69.8, 72.8, 112.2, 112.3, 115.9, 117.7, 120.8, 123.7, 124.2, 124.3, 124.4, 125.9, 127.0,

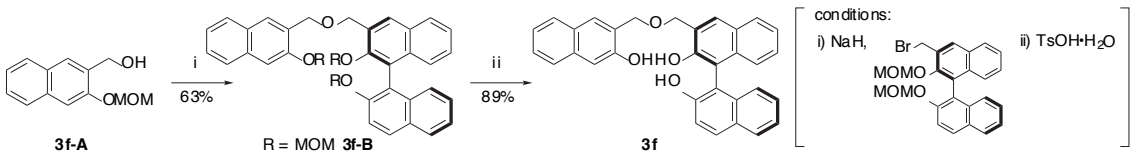
127.3, 127.4, 127.8, 128.2, 128.3, 128.7, 128.8, 128.9, 129.1, 129.3, 129.3, 129.3, 130.2, 130.8, 133.3, 133.4, 137.5, 138.4, 151.7, 152.1, 152.4; ESI-MS *m/z* 521 $[M+Na]^+$; $[\alpha]_D^{23}$ –20.5 (*c* 0.99, $CHCl_3$); HRMS (FAB): *m/z* calcd for $C_{34}H_{26}O_4$ $[M]^+$: 498.1831; found: 498.1838.



3e-A R = MOM 3e-B 3e

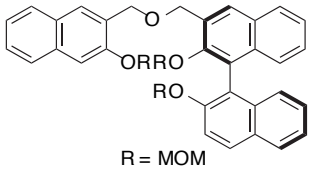


(*S*)-3-(2-Hydroxy-benzyloxymethyl)-1,1'-bi-2-naphthol: To a solution of alcohol **3e-A** (693 mg, 4.12 mmol) in THF (20 mL)/DMF (25 mL) at 0 ℃ was added NaH (60% purity, 198 mg, 4.94 mmol). The mixture was stirred at 0 ℃ for 30 min, then (*S*)-bromomethyl-MOM-BINOL (2.02 g, 4.33 mmol) was added. After stirring at room temperature over night, the mixture was quenched with H_2O, and extracted with diethyl ether (x 3). The organic layers were washed with H_2O, brine, and dried over Na_2SO_4. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 4/1 to 1/1) to give **3e-B** (2.16 g, y. 95%) as colorless oil. A mixture of **3e-B** (2.16 g, 3.89 mmol) and TsOH•H_2O (315 mg, 1.66 mmol) in CH_2Cl_2 (10 mL)/MeOH (10 mL) was stirred at 40 ℃ for over night. The mixture was diluted with CH_2Cl_2, and washed with *sat. aq*. $NaHCO_3$, brine. The organic layer was dried over Na_2SO_4. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 4/1 to 2/1) to give **3e** (1.31 g), and was recrystallized from CH_2Cl_2 /hexane to give **3e** (1.06 g, y. 65%) as colorless powder; IR (KBr) ν 3481, 3407, 3057, 1214, 754 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.82 (s, 2H), 4.86 (d, *J* = 12 Hz, 1H), 4.92 (d, *J* = 12 Hz, 1H), 5.11 (s, 1H), 5.80 (s, 1H), 6.75-6.90 (m, 2H), 7.05-7.40 (m, 10H), 7.80-8.00 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 69.6, 71.8, 111.0, 112.0, 116.5, 117.8, 120.0, 122.3, 123.9, 124.2, 124.3, 124.4, 125.2, 127.4, 127.6, 128.4, 128.7, 128.9, 129.4, 129.7, 130.6, 131.3, 133.3, 133.4, 151.3, 152.5, 156.0; ESI-MS *m/z* 445 $[M+Na]^+$; $[\alpha]_D^{22}$ –38.8 (*c* x1.12, $CHCl_3$); HRMS (FAB): *m/z* calcd for $C_{28}H_{22}O_4$ $[M]^+$: 422.1518; found: 422.1505.



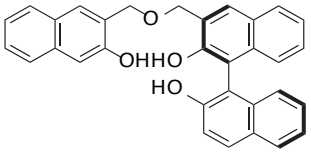
3f-A R = MOM 3f-B 3f

(*S*)-2,2'-Bis(methoxymethyloxy)-3-(3-methoxymethyloxy-naphthalen-2-ylmethoxymethyl)-1,1'-binaphthalene:

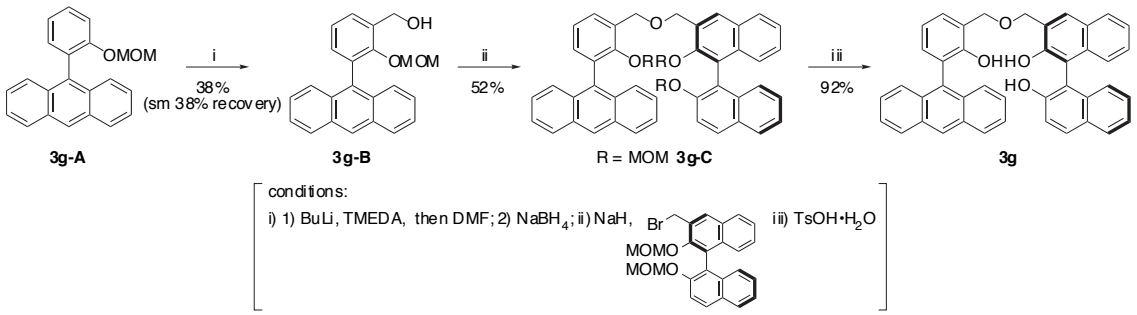


To a solution of alcohol **3f-A** (764 mg, 3.5 mmol) in DMF (30 mL) at 0 ℃ was added NaH (60% purity, 101 mg, 4.2 mmol). The mixture was stirred at 0 ℃ for 30 min, then (*S*)-bromomethyl-MOM-BINOL (1.96 g, 4.2 mmol) was added. After stirring at room temperature over night, the mixture was quenched with *sat. aq.* NH_4Cl extracted with diethyl ether (x 3). The organic layers were washed with H_2O, brine, and dried over Na_2SO_4 and $MgSO_4$. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 10/1 to 5/1) to give **3f-B** (1.32 g, y. 63%) as colorless foam; IR (KBr) ν 2900, 1151 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.82 (s, 3H), 3.14 (s, 3H), 3.50 (s, 3H), 4.58 (d, *J* = 5.5 Hz, 1H), 4.67 (d, *J* = 5.5 Hz, 1H), 4.96 (s, 2H), 5.01 (d, *J* = 7.0 Hz, 1H), 5.04 (s, 2H), 5.11 (d, *J* = 7.0 Hz, 1H), 5.34 (s, 2H), 7.15-7.45 (m, 9H), 7.57 (d, *J* = 8.9 Hz, 1H), 7.70-8.00 (m, 5H), 8.01 (s, 1H), 8.18 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 55.9, 56.1, 56.4, 68.3, 68.6, 94.4, 94.8, 99.3, 108.7, 116.5, 120.7, 124.1, 124.9, 125.3, 125.5, 125.7, 126.0, 126.1, 126.6, 126.7, 127.6, 127.8, 127.9, 127.9, 128.3, 128.5, 129.1, 129.6, 129.8, 130.9, 131.9, 133.4, 133.9, 134.0. 151.8, 152.8, 153.1; ESI-MS *m/z* 627 $[M+Na]^+$; HRMS (FAB): *m/z* calcd for $C_{38}H_{36}O_7$ $[M]^+$: 604.2461; found: 604.2454.

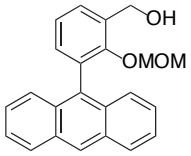
(*S*)-3-(3-Hydroxy-naphthalen-2-ylmethoxymethyl)-1,1'-bi-2-naphthol:



A mixture of **3f-B** (1.21 g, 2 mmol) and $TsOH•H_2O$ (76 mg, 0.4 mmol) in CH_2Cl_2 (25 mL)/MeOH (25 mL) was stirred at 40 ℃. After completion of the reaction checked by TLC, the mixture was quenched with *sat. aq.* $NaHCO_3$. The mixture was extracted with ethyl acetate (x 3). The organic layer was washed with brine, and was dried over Na_2SO_4. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 5/1) to give **3f** (0.842 g, y. 89%) as colorless powder; IR (KBr) ν 3483, 3383, 3055, 1107, 749 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.87 (d, *J* = 12 Hz, 1H), 4.93 (s, 2H), 4.93 (d, *J* = 12 Hz, 1H), 5.19 (s, 1H), 5.95 (s, 1H), 7.05-7.15 (m, 3H), 7.20-7.45 (m, 8H), 7.55-7.75 (m, 3H), 7.80-7.95 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 69.7, 71.8, 111.1, 111.2, 112.2, 117.8, 123.6, 123.9, 124.2, 124.3, 124.4, 124.8, 125.1, 126.3, 126.5, 127.3, 127.5, 127.6, 128.3, 128.3, 128.3, 128.9, 129.3, 130.6, 131.2, 133.3, 133.5, 134.7, 151.4, 152.5, 153.7; ESI-MS *m/z* 495 $[M+Na]^+$; $[\alpha]_D^{23}$ –52.4 (*c* 1.04, $CHCl_3$); HRMS (FAB): *m/z* calcd for $C_{32}H_{24}O_4$ $[M]^+$: 472.1675; found: 472.1664.

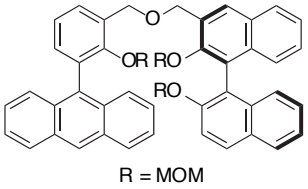


3-(9-Anthracenyl)-2-(methoxymethyloxy)benzyl alcohol:



To a stirred solution of compound **3g-A** (1.89 g, 6 mmol) and TMEDA (1.2 mL, 7.92 mmol) in THF (30 mL) at –78 ℃ was added BuLi (1.58 M in hexane, 7.6 mL, 12 mmol). After stirring at 0 ℃ for 30 min, the mixture was cooled down to –78 ℃ again. DMF (1.2 mL, 15 mmol) was added and was stirred at –78 ℃ for 4 h. Then, the mixture was quenched with *sat. aq.* NH_4Cl. The mixture was extracted with ethyl acetate (x 3). Organic layers were washed with brine, dried over Na_2SO_4, and evaporated to give aldehyde as a crude material. The crude aldehyde was dissolved in THF (20 mL)/MeOH (8 mL), and the solution was cooled at 0 ℃. $NaBH_4$ (227 mg, 6 mmol) was added, and the reaction mixture was stirred at 0 ℃ for over night. The reaction mixture was quenched with H_2O, and extracted with diethyl ether (x 3). The organic layers were washed with brine, dried over Na_2SO_4 and $MgSO_4$. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 10/1 to 2/1) to give alcohol **3g-B** (785 mg, y. 38%, 30% of **3g-A** recovered) as pale yellow viscous oil; IR (KBr) ν 3408, 3050, 2933, 1155 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.96 (s, 3H), 3.37 (t, J = 6.3 Hz, 1H), 4.16 (s, 2H), 4.81 (d, J = 6.3 Hz, 2H), 7.25-7.50 (m, 6H), 7.57 (dd, J = 1.7, 7.4 Hz, 1H), 7.64 (d, J = 9.2 Hz, 2H), 8.02 (d, J = 8.6 Hz, 2H), 8.49 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 56.8, 61.4, 98.7, 124.8, 125.2, 125.8, 126.4, 127.1, 128.4, 130.0, 130.1, 131.2, 131.8, 132.7, 133.1, 135.2, 155.0; ESI-MS *m/z* 367 $[M+Na]^+$; HRMS (FAB): *m/z* calcd for $C_{23}H_{20}O_3$ $[M]^+$: 344.1412; found: 344.1406.

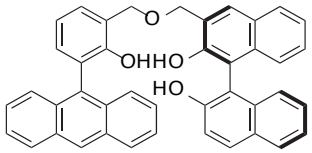
(*S*)-3-[3-(Anthracen-9-yl)-2-(methoxymethyloxy)benzyloxymethyl]-2,2'-bis(methoxymethyloxy)-1,1'-binaphthalene:

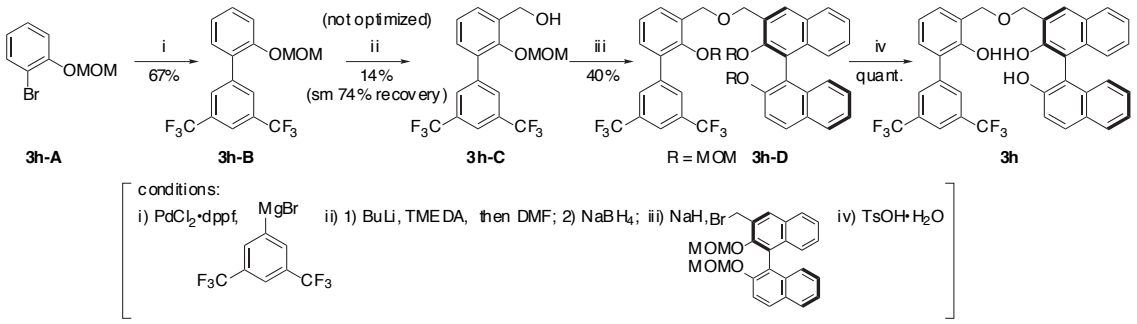


To a solution of alcohol **3g-B** (424 mg, 1.23 mmol) in DMF (10 mL) at 0 ℃ was added NaH (60% purity, 104 mg, 2.6 mmol). The mixture was stirred at 0 ℃ for 30 min, then (*S*)-bromomethyl-MOM-BINOL (690 mg, 1.47 mmol) was added. After stirring at room temperature for overnight, and the mixture was quenched with *sat. aq.* NH_4Cl, and extracted with CH_2Cl_2 (x 3). The organic layers were washed with H_2O, brine,

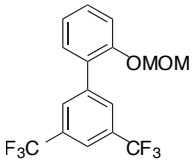
and dried over Na_2SO_4. After evaporation, the residue was purified by silica gel flash column choromatography (hexane/ethyl acetate = 10/1 to 5/1) to give **3g-C** (324 mg, y. 52%) as colorless oil; IR (KBr) ν 3053, 2928, 1154 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.45 (s, 3H), 2.88 (s, 3H), 3.15 (s, 3H), 4.32 (s, 2H), 4.61 (d, *J* = 5.8 Hz, 1H), 4.70 (d, *J* = 5.8 Hz, 1H), 5.00 (s, 2H), 5.02 (d, *J* = 7.5Hz, 1H), 5.07 (s, 2H), 5.13 (d, *J* = 7.5Hz, 1H), 7.15-7.75 (m, 16H), 7.75-8.10 (m, 6H), 8.19 (s, 1H), 8.50 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 55.9, 56.3, 56.6, 68.1, 68.7, 94.8, 99.0, 99.3, 116.4, 120.7, 124.1, 124.5, 125.0, 125.1, 125.3, 125.4, 125.7, 125.7, 126.0, 126.7, 126.9, 127.8, 128.0, 128.3, 128.4, 129.5, 129.6, 129.8, 130.3, 130.9, 131.3, 131.8, 131.9, 132.6, 132.8, 133.2, 133.4, 134.0, 151.8, 152.8, 153.8; ESI-MS *m/z* 753 $[M+Na]^+$; HRMS (FAB): *m/z* calcd for $C_{48}H_{42}O_7$ $[M]^+$: 730.2931; found: 730.2941.

(*S*)-3-[3-(Anthracen-9-yl)-2-hydroxybenzyloxymethyl]-1,1'-bi-2-naphthol: A mixture of **3g-C** (658 mg, 0.9 mmol) and $TsOH•H_2O$ (34 mg, 0.18 mmol) in CH_2Cl_2 (10 mL)/MeOH (10 mL) was stirred at 40 ℃. After 23 h, *sat. aq*. $NaHCO_3$ was added, and the mixture was extracted with ethyl acetate (x 3). The organic layers were washed with brine, and dried over Na_2SO_4. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 5/1 to 4/1) to give **3g** (497 mg, y. 92%) as colorless powder; IR (KBr) ν 3530, 3509, 3457, 3332, 3055, 752, 738 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.90 (d, *J* = 12 Hz, 1H), 4.92 (d, *J* = 12 Hz, 1H), 4.96 (s, 2H), 5.00 (s, 1H), 6.06 (s, 1H), 6.40 (s, 1H), 7.00-7.50 (m, 14H), 7.55-7.70 (m, 2H), 7.75-7.90 (m, 3H), 7.89 (s, 1H), 8.00 (d, *J* = 8.6 Hz, 2H), 8.48 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 70.3, 70.4, 112.2, 112.4, 117.6, 120.2, 123.3, 123.6, 124.1, 124.3, 124.3, 125.1, 125.3, 125.5, 125.9, 126.0, 126.2, 126.2, 127.0, 127.3, 127.5, 128.2, 128.2, 128.4, 128.5, 128.8, 129.2, 129.5, 130.0, 130.5, 130.5, 130.7, 130.7, 131.4, 131.4, 132.7, 133.3, 133.5, 152.0, 152.0, 153.3; ESI-MS *m/z* 621 $[M+Na]^+$; $[\alpha]_D^{25}$ –19.2 (*c* 0.99, $CHCl_3$); HRMS (FAB): *m/z* calcd for $C_{42}H_{30}O_4$ $[M]^+$: 598.2144; found: 598.2140.



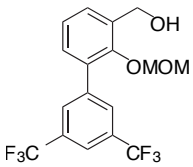


3',5'-Bis(trifluoromethyl)-2-methoxymethyloxybiphenyl:



To a mixture of $PdCl_2$•dppf (54.9 mg, 0.075 mmol) and **3h-A** (6.51 g, 30 mmol) in THF (50 mL) at room temperature was added Grignard reagent prepared from 3,5-bis(trifluoromethyl)-bromo benzene (9.67 g, 33 mmol) and Mg (1.2 g, 49.5 mmmol) in THF (40 mL). The mixture was stirred at 50 ℃ for 63 h, then MeOH (10 mL) and *sat. aq.* $NaHCO_3$ was added. The mixture was extracted with diethyl ether (x 3). The organic layers were washed with brine, and dried over Na_2SO_4 and $MgSO_4$ The residue was purified by silica gel flash column chromatography (hexane only) to give **3h-B** (7.09 g, y. 67%) as colorless solid; IR (KBr) ν 3072, 2972, 2835, 1279 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.41 (s, 3H), 5.17 (s, 2H), 7.05-7.50 (m, 4H), 7.84 (s, 1H), 8.00 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 56.3, 94.8, 115.1, 120.6 (sept, $^3J_{(C\text{-}F)}$ = 3.6 Hz), 122.4, 123.5 (q, $^1J_{(C\text{-}F)}$ = 273 Hz), 128.4, 129.7 (q, $^3J_{(C\text{-}F)}$ = 3.6 Hz), 130.2, 130.6, 131.2 (q, $^2J_{(C\text{-}F)}$ = 33.5 Hz), 140.5, 154.0; ESI-MS *m/z* 459 $[M+Ag]^+$; HRMS (FAB): *m/z* calcd for $C_{16}H_{12}F_6O_2$ $[M]^+$: 350.0741; found: 350.0742.

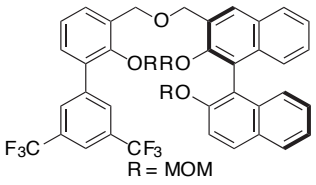
(3',5'-Di-trifluoromethyl-2-methoxymethyloxy-biphenyl-3-yl)-methanol:



To a stirred solution of compound **3h-B** (5.95 g, 17 mmol) and TMEDA (3.4 mL, 22.4 mmol) in THF (85 mL) at –78 ℃ was added BuLi (1.58 M in hexane, 12.9 mL, 20.4 mmol). After stirring at 0 ℃ for 1 h, the mixture was cooled down to –78 ℃ again. DMF (1.58 mL, 20.4 mmol) was added and was stirred at –78 ℃ to 0 ℃ over 1.5 h. Then, the mixture was quenched with *sat. aq.* NH_4Cl. The mixture was extracted with ethyl acetate (x 3). Organic layers were washed with brine, dried over Na_2SO_4, and evaporated to give aldehyde as a crude material. The crude aldehyde was dissolved in THF (55 mL)/MeOH (20 mL), and the solution was cooled at 0 °C. $NaBH_4$ (643 mg, 17 mmol) was added, and the reaction mixture was stirred at 0 ℃ for 2 h. The reaction mixture was quenched with H_2O, extracted with diethyl ether (x 3). The organic layers were washed with brine, dried over Na_2SO_4 and $MgSO_4$. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 10/1 to 4/1) to give alcohol **3h-C** (931 mg, y. 14%, 71% of **3h-B** recovered) as colorless viscous oil; IR (neat) ν 3407, 2942, 1279, 1132 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.08 (brs, 1H), 3.35 (s, 32H), 4.60 (s, 2H), 4.74 (brs, 2H), 7.28 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.35 (dd, *J* = 1.7, 7.5 Hz, 1H), 7.49 (dd, *J* = 1.7, 7.5 Hz, 1H), 7.87 (s, 1H), 8.04 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 57.4, 60.9, 99.8, 121.0 (sept, $^3J_{(C\text{-}F)}$ = 3.6 Hz), 123.3

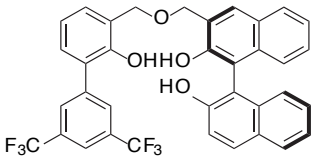
(q, $^{1}J_{(C\text{-}F)}$ = 274 Hz), 125.6, 129.4 (q, $^{3}J_{(C\text{-}F)}$ = 2.4 Hz), 130.6, 130.9, 131.8 (q, $^{2}J_{(C\text{-}F)}$ = 33.5 Hz), 132.3, 135.7, 140.6, 153.5; ESI-MS *m/z* 403 $[M+Na]^{+}$; HRMS (FAB): *m/z* calcd for $C_{17}H_{14}F_6O_3$ $[M]^{+}$: 380.0847; found: 380.0841.

(*S*)-2,2'-Bis(methoxymethyloxy)-3-[3',5'-di-trifluoromethyl-2-(methoxymethyloxy)biphenyl-3-ylmethoxymethyl]-1,1'-binaphthalene:



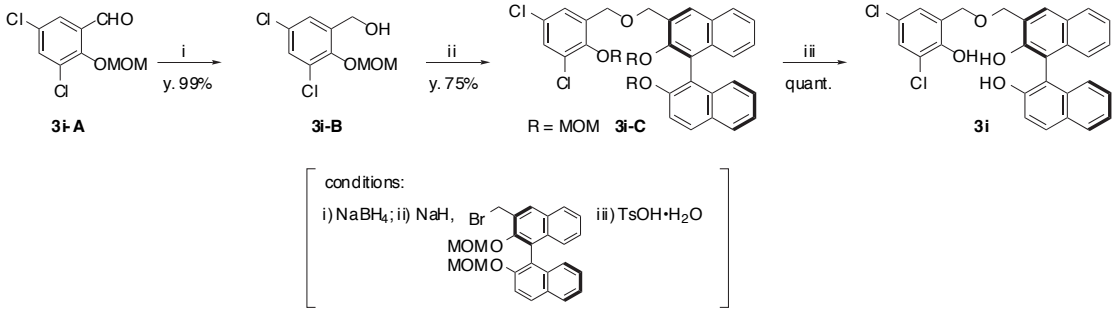
To a solution of alcohol **3h-C** (761 mg, 2 mmol) in DMF (20 mL) at 0 ℃ was added NaH (60% purity, 96 mg, 2.4 mmol). The mixture was stirred at 0 ℃ for 30 min, then (*S*)-bromomethyl-MOM-BINOL (1.40 g, 3 mmol) was added. After stirring at room temperature for 32 h, the mixture was quenched with *sat. aq*. NH_4Cl extracted with diethyl ether (x 3). The organic layers were washed with H_2O, brine, and dried over Na_2SO_4 and $MgSO_4$. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 10/1) to give **3h-D** (0.615 g, y. 40%) as colorless foam; IR (KBr) ν 3061, 2935, 1280, 1134 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.88 (s, 3H), 3.08 (s, 3H), 3.16 (s, 3H), 4.58 (d, *J* = 4.6 Hz, 1H), 4.67 (d, *J* = 4.6 Hz, 1H), 4.70 (s, 2H), 4.88 (s, 2H), 5.01 (s, 2H), 5.02 (d, *J* = 6.9Hz, 1H), 5.13 (d, *J* = 6.9Hz, 1H), 7.15-7.45 (m, 8H), 7.59 (d, *J* = 8.6Hz, 1H), 7.69 (dd, *J* = 1.7, 7.4Hz, 1H), 7.80-8.00 (m, 4H), 8.05 (s, 2H), 8.13 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 55.9, 56.6, 57.1, 67.8, 68.6, 94.8, 99.3, 100.4, 116.4, 120.6, 120.7, 123.3 (q, $^{1}J_{(C\text{-}F)}$ = 274 Hz), 124.1, 125.0, 125.1, 125.4, 125.5, 125.7, 126.1, 126.7, 127.9, 127.9, 128.4, 129.6, 129.7 (brq, $^{3}J_{(C\text{-}F)}$ = 2.4 Hz), 129.9, 130.2, 130.8, 130.9, 131.5 (q, $^{2}J_{(C\text{-}F)}$ = 33.5 Hz), 131.6, 132.8, 132.9, 133.5, 133.9, 141.0, 151.8, 152.8, 153.0; ESI-MS *m/z* 753 $[M+Na]^{+}$; HRMS (FAB): *m/z* calcd for $C_{42}H_{36}F_6O_7$ $[M]^{+}$: 766.2365; found: 766.2354.

(*S*)-3-(3',5'-Di-trifluoromethyl-2-hydroxybiphenyl-3-ylmethoxymethyl)-1,1'-bi-2-naphthol:

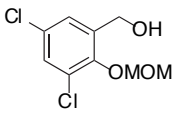


A mixture of **3h-D** (539 mg, 0.70 mmol) and $TsOH•H_2O$ (27 mg, 0.14 mmol) in CH_2Cl_2 (10 mL)/MeOH (10 mL) was stirred at 40 ℃. After 10 h, *sat. aq*. $NaHCO_3$ was added, and the mixture was extracted with ethyl acetate (x 3). The organic layers were washed with brine, and dried over Na_2SO_4. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 5/1) to give **3h** (473 mg, y. quant.) as colorless foam; IR (KBr) ν 3511, 3388, 1279, 1178, 1134 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.91 (d, *J* = 12 Hz, 1H), 4.92 (s, 2H), 4.99 (d, *J* = 12 Hz, 1H), 5.01 (s, 1H), 5.47 (s, 1H), 6.90-7.45 (m, 10H), 7.80 (s, 1H), 7.80-7.90 (m, 2H), 7.95 (s, 1H), 7.95 (d, *J* = 9.2 Hz, 1H), 7.99 (s, 1H), 7.99 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 69.6, 72.1, 110.4, 111.9, 117.8, 120.4, 120.6 (sept, $^{3}J_{(C\text{-}F)}$ = 3.6 Hz), 123.2, 123.5 (q, $^{1}J_{(C\text{-}F)}$ =

274 Hz), 124.0, 124.1, 124.2, 124.5, 124.9, 126.5, 127.5, 127.8, 128.4, 128.4, 128.9, 129.1, 129.4, 129.6 (brq, $^{3}J_{(C\text{-}F)}$ = 2.4 Hz), 130.6, 131.0, 131.52 (q, $^{2}J_{(C\text{-}F)}$ = 33.5 Hz), 131.6, 133.2, 133.4, 140.1, 151.0, 152.7, 153.4; ESI-MS *m/z* 657 $[M+Na]^+$; $[\alpha]_D^{23}$ –30.4 (*c* 0.98, $CHCl_3$); HRMS (FAB): *m/z* calcd for $C_{36}H_{24}F_6O_4$ $[M]^+$: 634.1579; found: 634.1584.

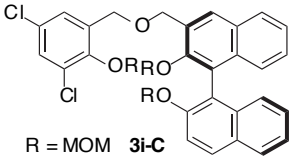


3,5-Dichloro-2-methoxymethyloxy-benzyl alcohol:



To a solution of aldehyde (5.88 g, 25 mmol) in THF (60 mL)/MeOH (25 mL) at 0 ℃ was added $NaBH_4$ (1.04 g, 27.5 mmol), and the reaction mixture was stirred at 0 ℃ for 2 h. The reaction mixture was quenched with H_2O, extracted with diethyl ether (x 3). The organic layers were washed with brine, dried over Na_2SO_4 and $MgSO_4$. After evaporation **3i-B** (5.90 g, y. 99%) was obtained as colorless solid; IR (KBr) ν 3291, 2949, 1162 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.26 (t, *J* = 7.0 Hz, 1H), 3.62 (s, 3H), 4.61 (d, *J* = 7.0 Hz, 2H), 5.09 (s, 2H), 7.29 (d, *J* = 2.5 Hz, 1H), 7.35 (d, *J* = 2.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 57.7, 60.3, 99.7, 128.2, 129.4, 130.2, 137.8, 150.7; ESI-MS *m/z* 260 $[M+Na]^+$; HRMS (FAB): *m/z* calcd for $C_9H_{10}Cl_2O_3$ $[M]^+$: 236.0007; found: 236.0006.

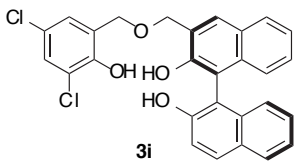
(*S*)-2,2'-Bis(methoxymethyloxy)-3-[3,5-dichloro-2-(methoxymethyloxy)benzyloxymethyl]-1,1'-binaphthalene:



To a solution of alcohol **3i-B** (948 mg, 4 mmol) in DMF (40 mL) at 0 ℃ was added NaH (60% purity, 192 mg, 4.8 mmol). The mixture was stirred at 0 ℃ for 30 min, then (*S*)-bromomethyl-MOM-BINOL (1.87 g, 4 mmol) was added. After stirring at room temperature for 12 h, the mixture was quenched with *sat. aq.* NH_4Cl, and extracted with diethyl ether (x 3). The organic layers were washed with H_2O, brine, and dried over Na_2SO_4 and $MgSO_4$. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 10/1) to give **3i-C** (1.86 g, y. 75%) as pale yellow viscous oil; IR (neat) ν 2932, 1158 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.88 (s, 3H), 3.15 (s, 3H), 3.55 (s, 3H), 4.54 (d, *J* = 5.8 Hz, 1H), 4.64 (d, *J* = 5.8 Hz, 1H), 4.82 (s, 2H), 4.96 (s, 2H), 5.03 (d, *J* = 7.4 Hz, 1H), 5.10 (s, 2H), 5.12 (d, *J* = 7.4 Hz, 1H), 7.10-7.55 (m, 9H), 7.57 (d, *J* = 9.2 Hz, 1H), 7.80-8.00 (m, 3H), 8.09 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 55.9, 56.6, 57.8, 67.3, 68.7, 94.8, 99.3, 100.0, 116.4, 120.5, 124.1,

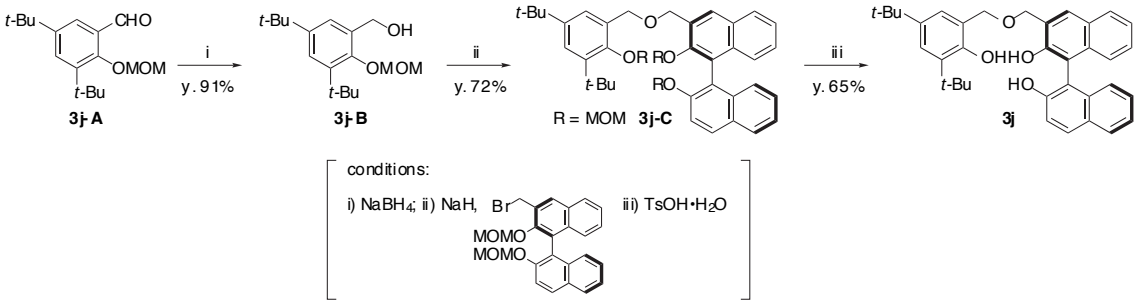
125.0, 125.4, 125.4, 125.7, 126.1, 126.7, 127.6, 127.9, 128.0, 128.2, 128.4, 129.1, 129.6, 129.9, 130.0, 130.8, 131.3, 133.5, 133.9, 135.6, 150.0, 151.8, 152.8; ESI-MS *m/z* 645 $[M+Na]^+$; HRMS (FAB): *m/z* calcd for $C_{34}H_{32}Cl_2O_7$ $[M]^+$: 622.1525; found: 622.1515.

(*S*)-3-(3,5-Dichloro-2-hydroxybenzyloxymethyl)-1,1'-bi-2-naphthol:

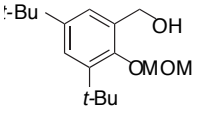


3i

A mixture of **3i-C** (1.57 g, 2.52 mmol) and $TsOH•H_2O$ (96 mg, 0.504 mmol) in CH_2Cl_2 (25 mL)/MeOH (25 mL) was stirred at 40 °C. After 24 h, *sat. aq.* $NaHCO_3$ was added, and the mixture was extracted with ethyl acetate (x 3). The organic layers were washed with brine, and dried over Na_2SO_4. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 5/1) to give **3i** (1.28 g, y. quant.) as colorless foam; IR (KBr) ν 3502, 3389, 3059, 1469, 1213, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.74 (s, 2H), 4.88 (d, *J* = 12 Hz, 1H), 4.92 (d, *J* = 12 Hz, 1H), 5.10 (s, 1H), 5.96 (s, 1H), 7.05-7.45 (m, 9H), 7.22 (s, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.93 (s, 1H), 7.94 (d, *J* = 9.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 69.8, 70.2, 111.2, 112.2, 117.8, 121.5, 123.9, 124.2, 124.3, 124.4, 124.8, 125.0, 125.4, 127.2, 127.3, 127.6, 128.3, 128.4, 128.9, 128.9, 129.4, 130.5, 131.2, 133.3, 133.5, 149.8, 151.4, 152.4; ESI-MS *m/z* 513 $[M+Na]^+$; $[\alpha]_D^{25}$ –43.0 (*c* 1.14, $CHCl_3$); HRMS (FAB): *m/z* calcd for $C_{28}H_{20}Cl_2O_4$ $[M]^+$: 490.0739; found: 490.0742.



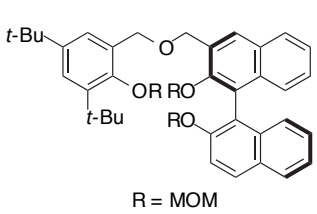
3,5-Di-*tert*-butyl-2-methoxymethyloxy-benzyl alcohol:



To a solution of aldehyde (5.57 g, 20 mmol) in THF (50 mL)/MeOH (20 mL) at 0 ℃ was added $NaBH_4$ (0.83 g, 22 mmol), and the reaction mixture was stirred at 0 ℃ to room temperature for over night. The reaction mixture was quenched with H_2O, and extracted with diethyl ether (x 3). The organic layers were washed with brine, and dried over Na_2SO_4. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 10/1 to 2/1) to give **3j-B** (5.11 g, y. 91%) as colorless oil; IR (neat) ν 3420, 2957, 1163 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.31 (s, 9H), 1.39 (s, 9H), 3.44 (brs, 1H), 3.69 (s, 3H), 4.58 (s, 2H), 4.98 (s, 2H), 7.28 (d, *J* = 2.3 Hz, 1H), 7.34 (d, *J* = 2.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 30.9, 31.2, 34.2, 34.8, 56.8, 61.6, 100.0, 124.1, 126.0, 134.0, 141.8, 146.4, 153.6; ESI-MS *m/z* 303 $[M+Na]^+$; HRMS (FAB): *m/z* calcd for $C_{17}H_{28}O_3$ $[M]^+$: 280.2038;

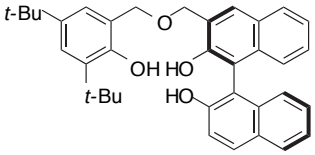
found: 280.2037.

(*S*)-2,2'-Bis(methoxymethyloxy)-3-[3,5-di-*tert*-butyl-2-(methoxymethyloxy)benzyloxymethyl]-1,1'-binaphthalene:

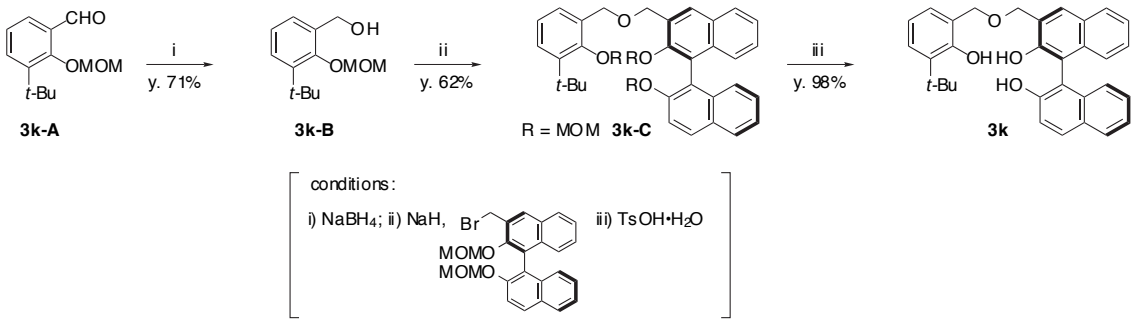


To a solution of alcohol **3j-B** (1.12 g, 4 mmol) in DMF (40 mL) at 0 ℃ was added NaH (60% purity, 192 mg, 4.8 mmol). The mixture was stirred at 0 ℃ for 30 min, then (*S*)-bromomethyl-MOM-BINOL (1.87 g, 4 mmol) was added. After stirring at room temperature for 10 h, the mixture was quenched with *sat. aq*. NH_4Cl, and extracted with diethyl ether (x 3). The organic layers were washed with H_2O, brine, and dried over Na_2SO_4 and $MgSO_4$. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 10/1) to give **3j-C** (1.91 g, y. 72%) as colorless viscous oil; IR (neat) ν 3060, 2958, 1161 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32 (s, 9H), 1.43 (s, 9H), 2.85 (s, 3H), 3.15 (s, 3H), 3.58 (s, 3H), 4.57 (d, *J* = 5.7 Hz, 1H), 4.65 (d, *J* = 5.7 Hz, 1H), 4.79 (s, 2H), 4.96 (s, 2H), 5.02 (d, *J* = 6.9 Hz, 1H), 5.09 (s, 2H), 5.11 (d, *J* = 6.9 Hz, 1H), 7.10-7.50 (m, 8H), 7.58 (d, *J* = 9.2 Hz, 1H), 7.80-8.00 (m, 3H), 8.12 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 31.0, 31.5, 34.5, 35.2, 55.9, 56.5, 57.1, 68.2, 69.0, 94.8, 99.2, 100.6, 116.4, 120.7, 124.1, 124.1, 124.9, 125.2, 125.5, 125.6, 125.9, 125.9, 126.7, 127.8, 127.9, 128.4, 129.6, 129.8, 130.6, 130.9, 132.0, 133.4, 134.0, 141.9, 145.96, 141.7, 152.8, 152.9; ESI-MS *m/z* 689 $[M+Na]^+$; HRMS (FAB): *m/z* calcd for $C_{42}H_{50}O_7Cs$ $[M+Cs]^+$: 799.2611; found: 799.2619.

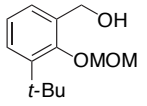
(*S*)-3-(3,5-Di-*tert*-butyl-2-hydoxybenzyloxymethyl)-1,1'-bi-2-naphthol:



To a solution of **3j-C** (1.67 g, 2.5 mmol) in CH_2Cl_2(45 mL)/MeOH (45 mL) at 0 ℃ was added conc. HCl (1.2 g). The mixture was stirred at room temperature. After 24 h, *sat. aq*. $NaHCO_3$ was added, and the mixture was extracted with ethyl acetate (x 3). The organic layers were washed with brine, and dried over Na_2SO_4. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 5/1) to give **3j** (863 mg, y. 65%) as colorless foam; IR (KBr) ν 3527, 3408, 2956, 1215, 750 cm^{-1}; ^1H NMR ($CDCl_3$) d 1.21 (s, 9H), 1.40 (s, 9H), 4.84 (s, 2H), 4.92 (s, 2H), 5.01 (s, 1H), 5.60 (s, 1H), 6.94 (d, *J* = 2.3 Hz, 1H), 7.13 (dd, *J* = 2.3, 8.6 Hz, 1H), 7.25-7.45 (m, 6H), 7.49 (s, 1H), 7.80-7.90 (m, 2H), 7.96 (d, *J* = 9.2 Hz, 1H), 7.96 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 29.6, 31.6, 34.2, 34.9, 69.0, 72.9, 110.8, 111.7, 117.8, 121.7, 123.5, 124.0, 124.1, 124.2, 124.2, 124.4, 125.3, 127.5, 127.6, 128.4, 128.4, 129.0, 129.4, 130.7, 131.4, 133.3, 133.3, 136.3, 141.5, 151.3, 152.6, 153.0; ESI-MS *m/z* 557 $[M+Na]^+$; $[\alpha]_D^{23}$ –49.7 (*c* 1.03, $CHCl_3$); HRMS (FAB): *m/z* calcd for $C_{36}H_{38}O_4$ $[M]^+$: 534.2770; found: 534.2759.

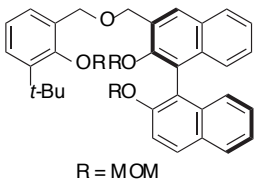


3-*tert*-Butyl-2-methoxymethyloxy-benzyl alcohol:



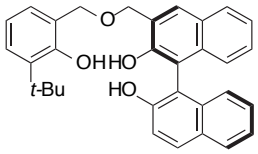
To a solution of aldehyde (1.56g, 7 mmol) in THF (20 mL)/MeOH (9 mL) at 0 ℃ was added $NaBH_4$ (0.29 g, 7.7 mmol), and the reaction mixture was stirred at 0 ℃ to room temperature for over night. The reaction mixture was quenched with H_2O, and was extracted with diethyl ether (x 3). The organic layers were washed with brine, and dried over Na_2SO_4. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 5/1) to give **3k-B** (1.11 g, y. 71%) as colorless oil; IR (neat) ν 3407, 2956, 1163 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.39 (s, 9H), 3.33 (brs, 1H), 3.68 (s, 3H), 4.60 (s, 2H), 4.99 (s, 2H), 7.07 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.28 (dd, *J* = 1.7, 8.0 Hz, 1H), 7.31 (dd, *J* = 1.7, 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 30.8, 34.6, 56.8, 61.1, 100.0, 124.1, 126.9, 129.1, 134.8, 142.7, 155.7; ESI-MS *m/z* 247 $[M+Na]^+$; HRMS (FAB): *m/z* calcd for $C_{13}H_{20}O_3$ $[M]^+$: 224.1412; found: 224.1415.

(*S*)-2,2'-Bis(methoxymethyloxy)-3-[3-*tert*-butyl-2-(methoxymethyloxy)benzyloxymethyl]-1,1'-binaphthalene:



To a solution of alcohol **3k-B** (897 mg, 4 mmol) in DMF (40 mL) at 0 ℃ was added NaH (60% purity, 192 mg, 4.8 mmol). The mixture was stirred at 0 ℃ for 30 min, then (*S*)-bromomethyl-MOM-BINOL (1.87 g, 4 mmol) was added. After stirring at room temperature for 10 h, the mixture was quenched with *sat. aq.* NH_4Cl, and extracted with diethyl ether (x 3). The organic layers were washed with H_2O, brine, and dried over Na_2SO_4 and $MgSO_4$. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 10/1 to 8/1) to give **3k-C** (1.52 g, y. 62%) as pale yellow viscous oil; IR (neat) ν 3060, 2955, 1159 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.43 (s, 9H), 2.84 (s, 3H), 3.15 (s, 3H), 3.59 (s, 3H), 4.57 (d, *J* = 5.5 Hz, 1H), 4.65 (d, *J* = 5.5 Hz, 1H), 4.81 (s, 2H), 4.95 (s, 2H), 5.01 (d, *J* = 6.8 Hz, 1H), 5.10 (s, 2H), 5.11 (d, *J* = 6.8 Hz, 1H), 7.05-7.50 (m, 9H), 7.58 (d, *J* = 9.2 Hz, 1H), 7.80-8.00 (m, 3H), 8.10 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 31.0, 35.0, 55.9, 56.5, 57.2, 68.3, 68.6, 94.8, 99.2, 100.7, 116.5, 120.7, 123.8, 124.1, 124.9, 125.2, 125.5, 125.6, 126.0, 126.6, 126.9, 127.8, 127.9, 128.4, 129.0, 129.6, 129.8, 130.9, 131.7, 131.9, 133.4, 134.0, 142.9, 151.7, 152.8, 155.2; ESI-MS *m/z* 633 $[M+Na]^+$; HRMS (FAB): *m/z* calcd for $C_{38}H_{42}O_7Cs$ $[M+Cs]^+$: 743.1985; found: 743.1992.

(*S*)-3-(3-*tert*-Butyl-2-hydoxybenzyloxymethyl)-1,1'-bi-2-naphthol:



To a solution of **3k-C** (1.34 g, 2.2 mmol) in CH_2Cl_2(40 mL)/MeOH (40 mL) at 0 ℃ was added conc. HCl (1.0 g). The mixture was stirred at room temperature. After 25 h, *sat. aq.* $NaHCO_3$ was added, and the mixture was extracted with ethyl acetate (x 3). The organic layers were washed with brine, and dried over Na_2SO_4. After evaporation, the residue was purified by silica gel flash column chromatography (hexane/ethyl acetate = 5/1) to give **3k** (1.03 g, y. 98%) as colorless foam; IR (KBr) ν 3503, 3398, 2955, 1214, 749 cm^{-1}; ^1H NMR ($CDCl_3$) d 1.39 (s, 9H), 4.84 (s, 2H), 4.90 (s, 2H), 5.03 (s, 1H), 5.55 (s, 1H), 6.80 (dd, *J* = 7.4, 8.1 Hz, 1H), 7.95 (dd, *J* = 1.2, 7.5 Hz, 1H), 7.10-7.45 (m, 8H), 7.70 (s, 1H), 7.85-7.90 (m, 2H), 7.96 (s, 1H), 7.96 (d, *J* = 9.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 29.5, 34.7, 68.8, 72.5, 110.8, 111.7, 117.8, 119.3, 122.5, 124.0, 124.1, 124.2, 124.4, 125.3, 126.7, 127.2, 127.5, 127.6, 128.4, 128.4, 129.0, 129.4, 130.8, 131.4, 133.3, 133.3, 137.1, 151.2, 152.6, 155.5 ; ESI-MS *m/z* 501 $[M+Na]^+$; $[\alpha]_D^{23}$ –58.0 (*c* 1.15, $CHCl_3$); HRMS (FAB): *m/z* calcd for $C_{32}H_{30}O_4$ $[M]^+$: 478.2144; found: 478.2142.

Procedure for Catalytic Asymmetric *anti*-Selective Mannich-type Reaction Promoted by Et_2Zn/(*S*)-ligand Complex (5 mol % ligand loading, Table 1):

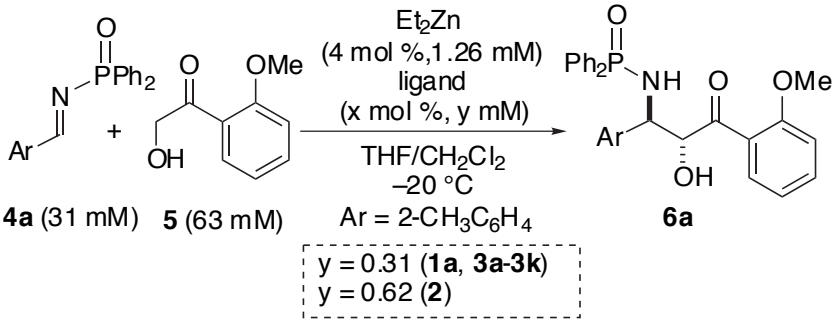
MS 3A (103 mg) in a flask was activated prior to use under reduced pressure (ca. 0.7 kPa) at 160 ℃ for 3 h. After cooling down to room temperature, argon gas was refilled and a solution of (*S*)-ligand **3** (0.025 mmol) in THF (0.83 mL) was charged. The mixture was cooled down to –20 °C. To this suspension was added Et_2Zn (100 μL, 0.1 mmol, 1.0 M in hexanes). After stirring for 10 min at -20 ℃, a solution of ketone **5** (166 mg, 1.0 mmol) in THF (1 mL) was added, and the mixture was stirred for 10 min at -20 °C. Then, a mixture solution of imine **4a** (160 mg, 0.5 mmol) in THF/CH_2Cl_2 (0.5 mL/1 mL) was added, and stirred at -20 ℃. The stirring was continued for indicated time in Table 1 until completion of the reaction and quenched by addition of saturated aqueous NH_4Cl. The mixture was extracted with ethyl acetate (x 3). The combined organic layers were washed with brine and dried over Na_2SO_4. Evaporation of solvent gave a crude mixture of the Mannich products. The diastereomeric ratio was determined by ^1H NMR analysis of the crude product. The crude mixture was purified by flash silica gel column chromatography (hexane/AcOEt = 1/1 to 0/1, then AcOEt/methanol = 9/1) and enantiomeric excess was determined by chiral HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/hexane 50/50, flow 0.3 mL/min, detection at 254 nm) t_R 15.0 min (major) and 20.4 min (minor).

General Procedure for Reaction Profile with Various Chiral Ligands under Diluted Conditions (Table 2 and Figure 5):

MS 3A (206 mg) in a flask was activated prior to use under reduced pressure (ca. 0.7 kPa) at 160 ℃ for 3 h. After cooling down to room temperature, argon gas was refilled and a solution of (*S*)-ligand **3** (0.01 mmol) in THF (0.333 mL) was charged. THF (16.5 mL)

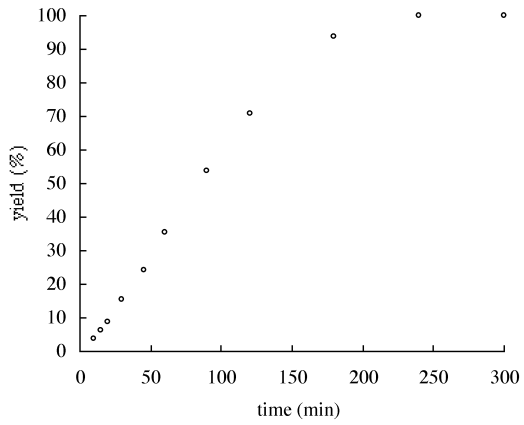
and CH_2Cl_2 (10 mL) were added to the flask. The mixture was cooled down to –20 °C. To this suspension was added Et_2Zn (40 μL, 0.04 mmol, 1.0 M in hexanes). After stirring for 10 min at –20 ℃, a solution of ketone **5** (332 mg, 2 mmol) in THF (2 mL) was added, and the mixture was stirred for 10 min at –20 °C. Then, a mixture solution of imine **4a** (319 mg, 1 mmol) in THF/CH_2Cl_2 (1 mL/2 mL) was added, and stirred at -20 ℃. Samples were taken at recorded times according to the following procedure: 0.1 mL of the reaction mixture was taken with a syringe filled with 0.3 mL of saturated aqueous NH_4Cl solution and was immediately poured onto saturated aqueous NH_4Cl (2.0 mL). The resulting mixture was extracted with ethyl acetate. After evaporating solvents, the crude residue was analyzed by ^1H NMR to determine yield. Initial reaction rate (mM/min) was calculated from data at the initial stage (yiled <30%) for each ligand.

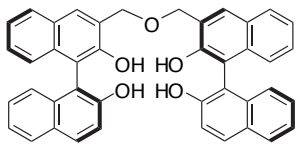
<standard conditions>



<Reaction profile under diluted conditions>

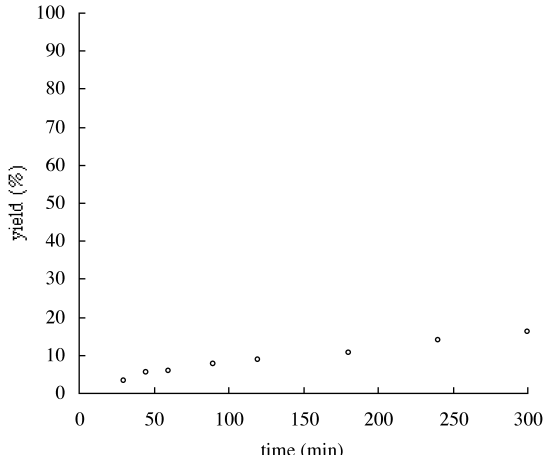
ligand **1a**: (0.31 mM, 1 mol %)

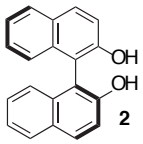




(*S*,*S*)-linked-BINOL **1a**

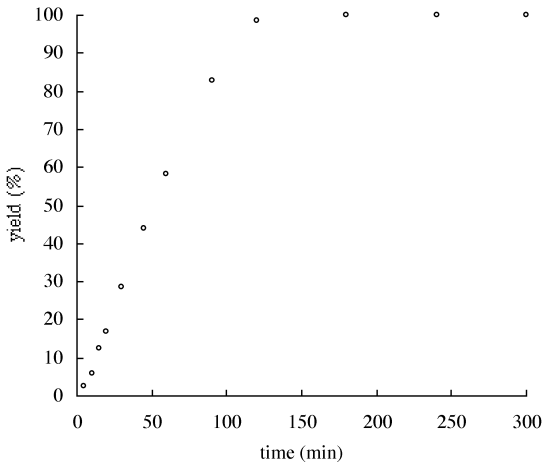
ligand **2**: (0.62 mM, 2 mol %)

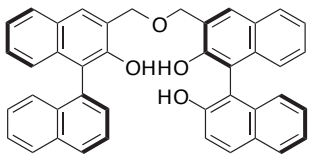




2

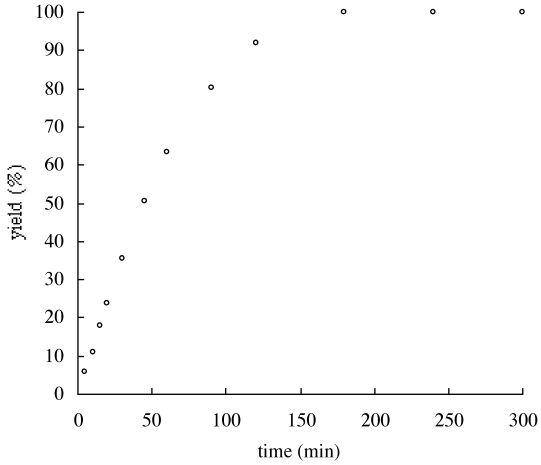
ligand **3a**: (0.31 mM, 1 mol %)

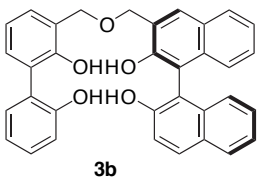




3a

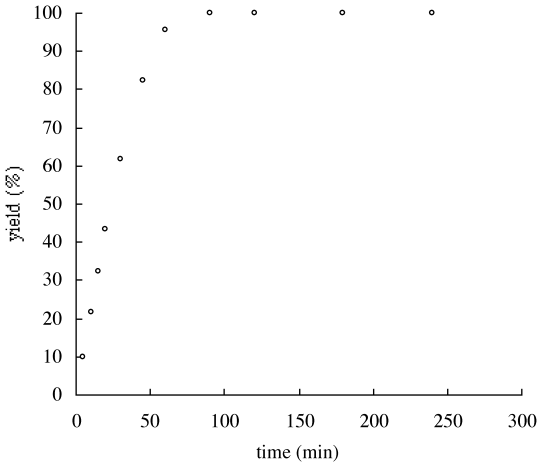
ligand **3b**: (0.31 mM, 1 mol %)

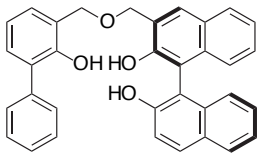




3b

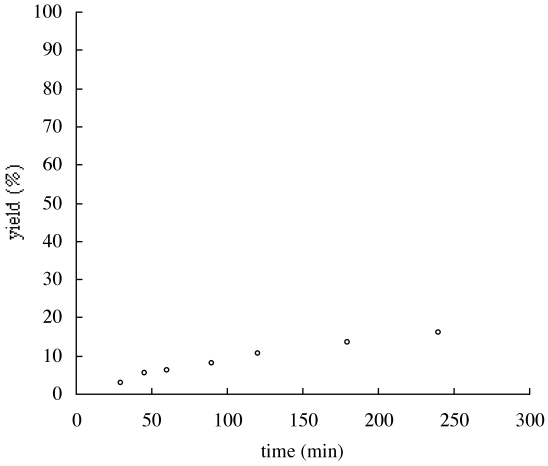
ligand **3c**: (0.31 mM, 1 mol %)

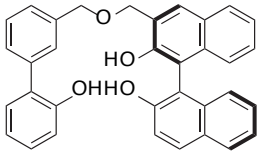




3c

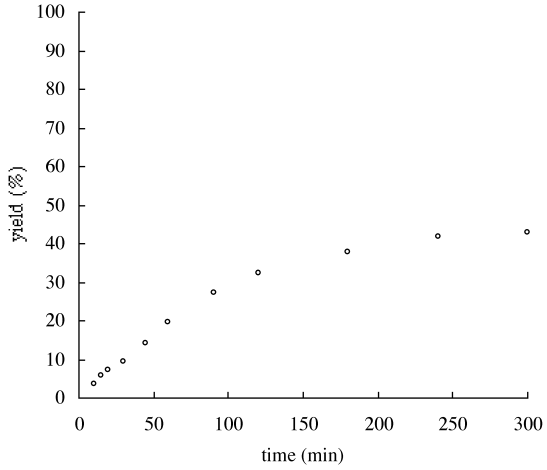
ligand **3d**: (0.31 mM, 1 mol %)

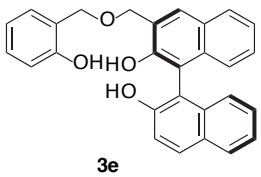




3d

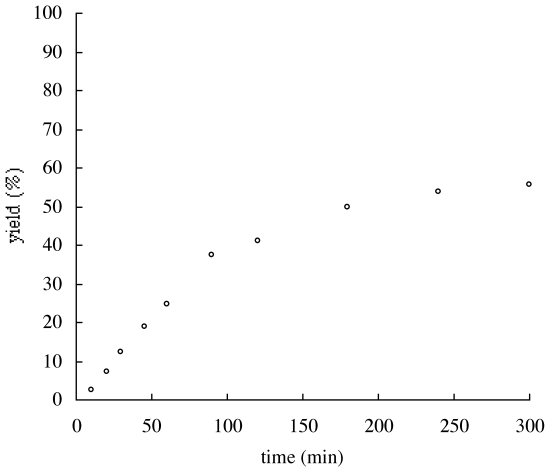
ligand **3e**: (0.31 mM, 1 mol %)

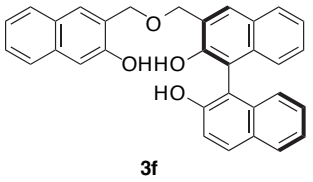




3e

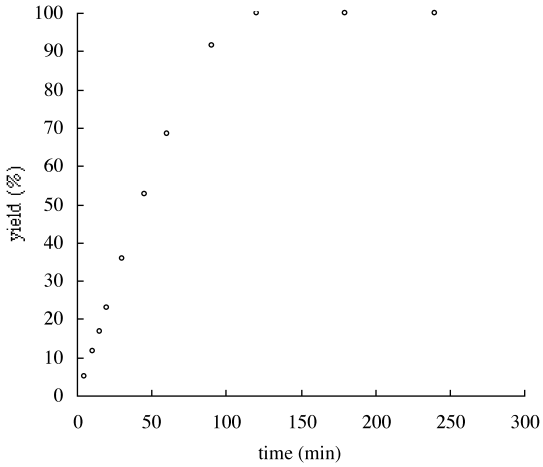
ligand **3f**: (0.31 mM, 1 mol %)

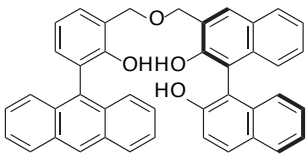




3f

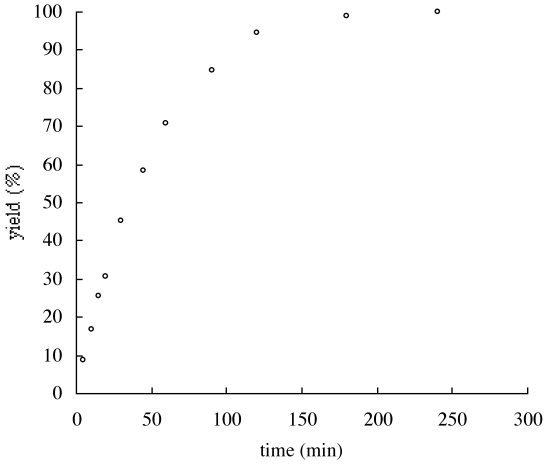
ligand **3g**: (0.31 mM, 1 mol %)

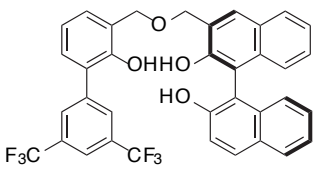




3g

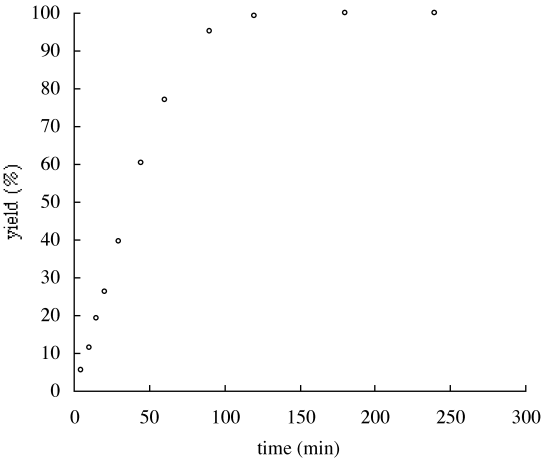
ligand **3h**: (0.31 mM, 1 mol %)

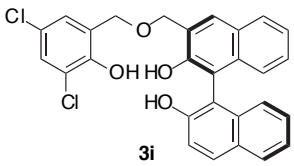




3h

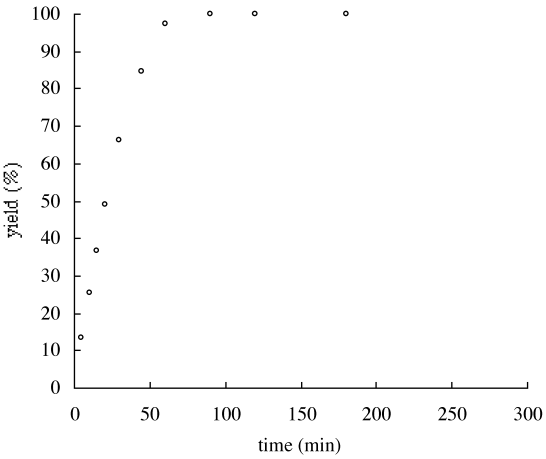
ligand **3i**: (0.31 mM, 1 mol %)

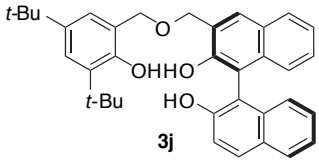




3i

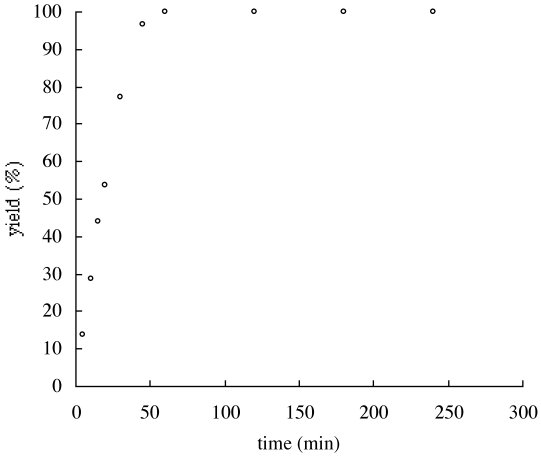
ligand **3j**: (0.31 mM, 1 mol %)

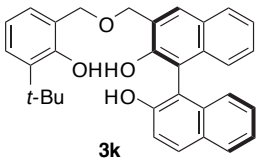




3j

ligand **3k**: (0.31 mM, 1 mol %)





3k

Procedure for Catalytic Asymmetric *anti*-Selective Mannich-type Reaction Promoted by Et_2Zn/(*S*)-ligand 3c Complex (0.01 mol % catalyst loading, Scheme 1):

MS 3A (5.0 g) in a flask was activated prior to use under reduced pressure (ca. 0.7 kPa) at 160 ℃ for 3 h. After cooling down to room temperature, argon gas was refilled and a solution of (*S*)-ligand **3c** (2.49 mg, 0.005 mmol) in THF (5.17 mL) was charged. To this suspension was added Et_2Zn (20 μL, 0.02 mmol, 1.0 M in hexanes). After stirring for 20 min at 0 ℃, a solution of **5** (1.66 g, 10 mmol) in THF (10 mL) was added, and the mixture was stirred for 25 min at 0 ℃. Then, a mixture solution of **5** (10.8 g, 65 mmol) and **4a** (15.97 g, 50 mmol) in THF/CH_2Cl_2 (20 mL/17.5 mL) was added, and stirred at 0 ℃ for 36 h.

Procedure for Catalytic Asymmetric *anti*-Selective Mannich-type Reaction Promoted by Et_2Zn/(*S*)-ligand 3c Complex (1 mol % catalyst loading, Scheme 2):

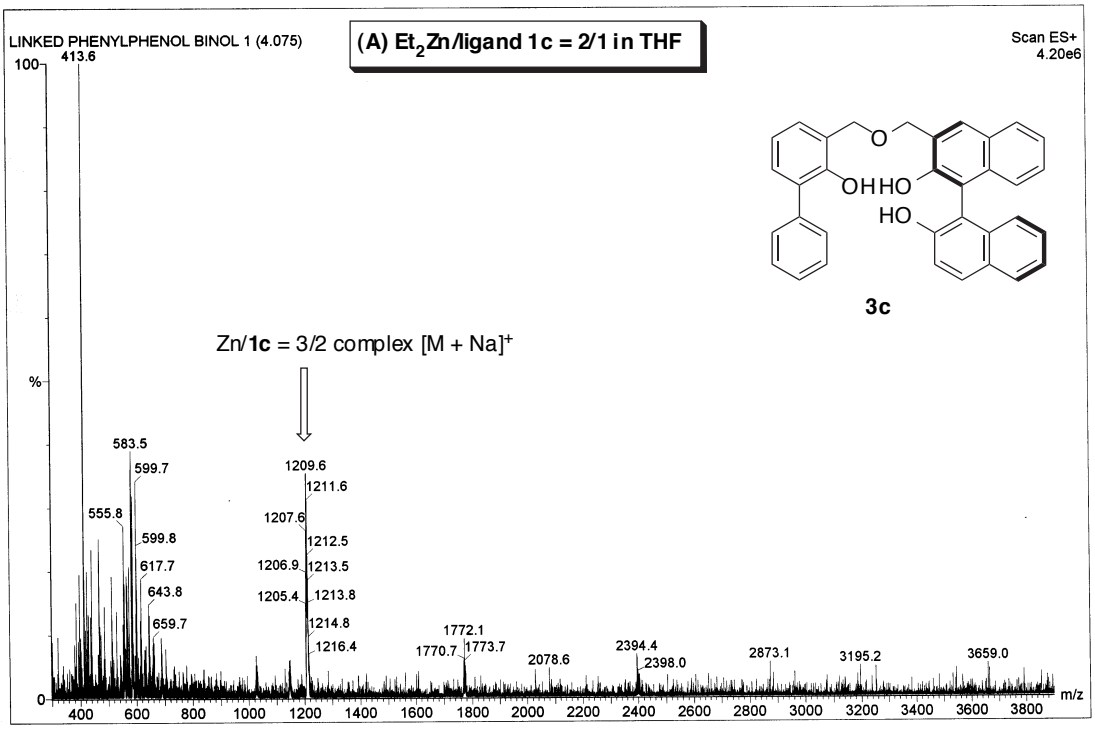
MS 3A (103 mg) in a test tube was activated prior to use under reduced pressure (ca. 0.7 kPa) at 160 ℃ for 3 h. After cooling down to room temperature, argon gas was refilled and a solution of (*S*)-**3c** (2.49 mg, 0.005 mmol) in THF (166 μL) was charged. To this suspension was added Et_2Zn (20 μL, 0.02 mmol, 1.0 M in hexanes). After stirring for 10 min at –20 ℃, a solution of **5** (166.17 mg, 1.0 mmol) in THF (1.0 mL) and imine (0.5 mmol) in THF (0.5 mL)/CH_2Cl_2 (1.0 mL) was added successively, and stirred at the same temperature for indicated time in Scheme 2.

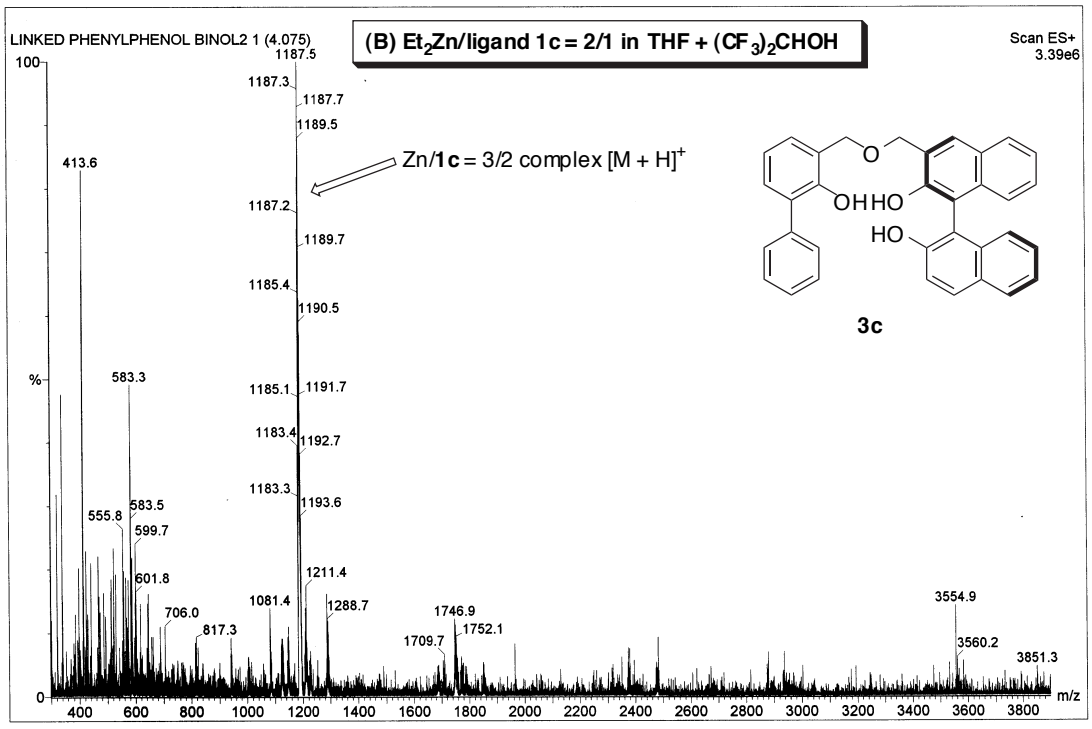
ESI-MS and NMR Charts of Et_2Zn/ligand 3c mixture

<ESI-MS analysis>
Sample preparation: Ligand **3c** (0.03 mmol, 15.7 mg, containg 4.6w/w% diethyl ether) was dissolved in THF (1 mL). To the solution was added Et_2Zn (60 μL, 0.06 mmol, 1.0 M in hexanes). The mixture was stirred at room temperature. From the Zn/**3c** solution, 0.25 mL was sampled and diluted with THF (5 mL) before injection to ESI-MS. In (A) THF solution was directly injected to give $[M+Na]^+$ peaks. In (B) sample was treated with $(CF_3)_2CHOH$ as a proton source to give $[M+H]^+$ peaks. Observed major peaks were assigned as Zn/**3c** = 3/2 complex. Peak distribution pattern matched well with zinc natural isotopes distribution pattern. Zn: 64 (48.89%), 66 (27.81%), 68 (18.57%), 67 (4.11%), 70 (0.62%).

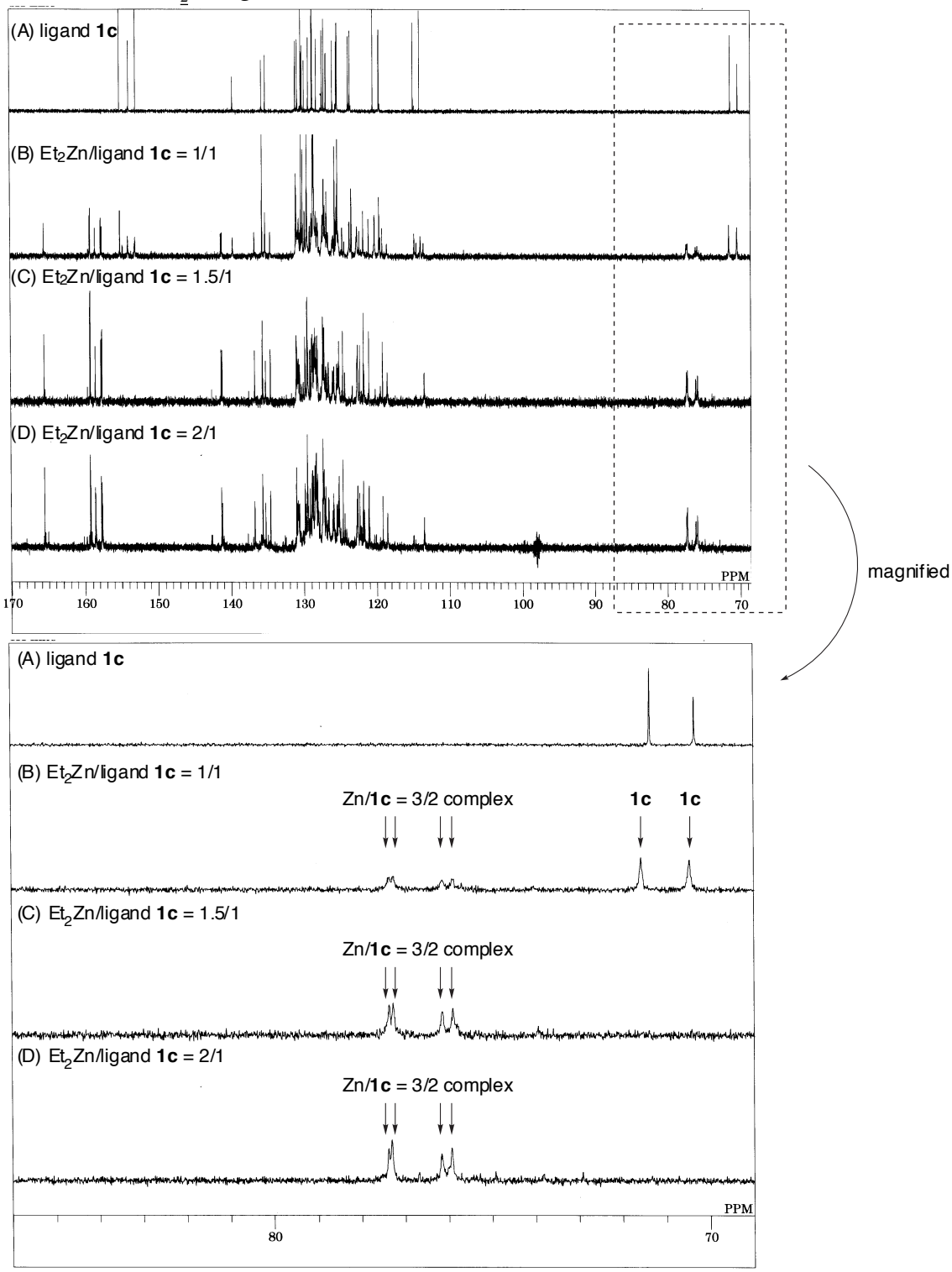
<NMR analysis>
Sample preparation: Ligand **3c** (0.275 mmol, 143.7 mg, containg 4.6w/w% diethyl ether) was dissolved in *d8*-THF (0.75 mL). To this solution, Et_2Zn (1.0 M in hexanes) were added. In four different benzylic carbon peaks and eight different proton peaks were observed, suggesting the non-C_2-symmetric structure of Zn/**3c** complex.

<ESI-MS charts of Et_2Zn/ligand **3c** = 2/1 mixture>





<^{13}C NMR Charts of (A) ligand **3c**, (B) Et_2Zn/ligand **1c** = 1/1, (C) Et_2Zn/ligand **1c** = 1.5/1, and (D) Et_2Zn/ligand **1c** = 2/1>



<^{1}H NMR Charts of (A) ligand **3c**, (B) Et_2Zn/ligand **1c** = 1/1, (C) Et_2Zn/ligand **1c** = 1.5/1, and (D) Et_2Zn/ligand **1c** = 2/1>