Catalytic Asymmetric Ring Opening of *meso*-Epoxides with Aromatic Amines in Water

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Supporting Information

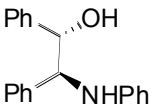
Instrumentation. Proton nuclear magnetic resonance (^{1}H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) were recorded on a JEOL JNM-LA400 (400 MHz) spectrometer. Chemical shifts for protons and carbons are reported in parts per million (ppm) downfield from tetramethylsilane as an internal standard. Data are presented as follows: chemical shift, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant in Hertz (Hz) and integration. Infrared (IR) spectra were obtained using a JASCO FT/IR-610 spectrophotometer. Data are represented as frequency of absorption (cm^{-1}). Optical rotations were measured using a 2 mL cell with a 1 dm path length on a JASCO P-1010 polarimeter. Data are reported as follows: $[\alpha]^t_D$ (c in g per 100 mL, solvent). Melting points were measured on a Yazawa Melting Point BY-I apparatus and are uncorrected. The mass spectroscopic data were obtained on a Bruker Daltonics BioTOF II spectrometer. Chiral HPLC analysis was performed on a Shimadzu VP-series instrument with a chiral stationary phase column as indicated.

Materials. Chiral bipyridine ligand **1** was prepared according to the reported procedure.[1] Aromatic epoxides **2d**, **2f** and **2g** were prepared by *m*CPBA oxidation of the corresponding *cis*-alkenes according to the reported procedure.[2] All other compounds were commercially available and used as received except aniline and substituted anilines which were distilled from calcium hydride before use. $Sc(DS)_3.3\,H_2O$ was purchased from Wako Chemicals. Preparative thin-layer chromatography (PTLC) was carried out using Wakogel B-5F. The corresponding racemic products were prepared using the achiral scandium-bipyridine complex as catalyst in order to secure the chiral HPLC-assay of the enantioselective reactions.

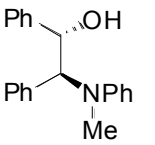
General Procedure for Catalytic Asymmetric Ring Opening of *meso*-Epoxides. All asymmetric ring opening reactions were conducted in deionised water under an atmosphere of argon. To a stirred solution of $Sc(DS)_3$ (0.01 equiv) in water (1 M concentration with respect of the substrates) was added the chiral bipyridine ligand **1** (0.012 equiv). The reaction mixture was stirred for one hour at room temperature (rt) upon which the amine and the epoxide were added. Vigorous stirring was continued for 30-48 h at rt. The reaction was quenched with saturated aqueous $NaHCO_3$. The resultant mixture was extracted with ethyl acetate (three times), and the combined organic layers were dried over anhydrous Na_2SO_4. The solvents were evaporated, and the residue was purified by PTLC over silica gel using mixtures of ether-hexane as eluent to give the pure amino alcohol. All known compounds were compared with data reported in the literature; all new compounds were fully

[1] Ishikawa, S.; Hamada, T.; Manabe, K.; Kobayashi, S. *Synlett* **2005**, in press.
[2] Lusinchi, X.; Hanquet, G. *Tetrahedron* **1997**, *53*, 13727

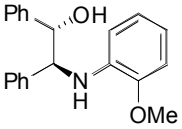
characterized. The absolute configuration of the products was assigned by comparison with the reported optical rotation values and for the unknown compounds by analogy.



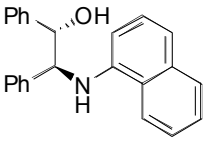
(1*S*,2*S*)-1,2-Diphenyl-2-(phenylamino)-ethanol (3a).[3] The title compound was isolated as a white solid; melting point: 100-102 °C. The ee was determined by HPLC using a Daicel Chiralpak AD column (19/1 hexane/*i*-PrOH; flow rate 1 mL/min; τ_{major} = 25.5 min; τ_{minor} = 29.8 min); ee = 91%. $[\alpha]^{24}_D$ = -45.2° (c = 0.520, CH_2Cl_2). **IR** (cm^{-1}): 3404, 3060, 1490, 1453, 1337, 1201, 1105, 1060. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 2.75 (br s, 1H), 4.46 (d, J = 6.0 Hz, 1H), 4.54 (br s, 1H), 4.74 (d, J = 6.0 Hz, 1H), 6.48-6.50 (m, 2H), 6.59-6.6 (m, 1H), 7.0-7.04 (m, 2H), 7.12-7.23 (m, 10H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 64.7, 78.0, 114.1, 117.8, 126.7, 127.2, 127.4, 127.8, 128.1, 128.4, 129.0, 140.1, 140.5, 147.2. **HRMS** (ESI): $[M+H]^+$ calcd. 290.1545, found 290.1537.



(1*S*,2*S*)-2-(*N*-Methyl-*N*-phenylamino)-1,2-diphenylethanol (3b). [4] The title compound was isolated as a white solid; melting point: 57-59 °C. The ee was determined by HPLC using a Daicel Chiralpak AS-H column (19/1 hexane/*i*-PrOH; flow rate 0.8 mL/min; τ_{minor} = 18.2 min; τ_{major} = 24.3 min); ee = 96%. $[\alpha]^{23}_D$ = +171.7° (c = 0.530, CH_2Cl_2). **IR** (cm^{-1}): 3415, 3060, 3030, 2887, 1597, 1499, 1452, 1320, 1190, 754, 698. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 2.68 (s, 3H), 3.96 (br s, 1H), 4.87 (d, J =10.1 Hz, 1H), 5.28 (d, J = 9.6 Hz, 1H), 6.88-6.92 (m, 1H), 6.96-7.01 (m, 4H), 7.11-7.29 (m, 8H), 7.38 (d, J =7.7 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 32.7, 71.5, 73.7, 117.8, 120.3, 127.6, 127.7, 127.9, 128.2, 128.8, 129.1, 134.6, 140.6, 151.3. **HRMS** (ESI): $[M+H]^+$ calcd. 304.1701, found 304.1691.



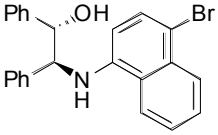
(1*S*,2*S*)-2-(2-Methoxyphenylamino)-1,2-diphenylethanol (3c). [5] The title compound was isolated as a white solid; melting point: 93-95 °C. The ee was determined by HPLC using a Daicel Chiralpak AS-H column (19/1 hexane/*i*-PrOH; flow rate 0.8 mL/min; τ_{major} = 26.9 min; τ_{minor} = 33.2 min); ee = 93%. $[\alpha]^{24}_D$ = -48.0° (c = 0.540, CH_2Cl_2). **IR** (cm^{-1}): 3398, 3061, 3028, 2934, 2857, 1608, 1509, 1455, 1225, 1027, 738, 701. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 2.75 (br s, 1H), 3.80 (s, 3H), 4.46 (d, J = 6.4 Hz, 1H), 4.78 (d, J = 6.4 Hz, 1H), 6.36 (dd, J = 7.8 Hz, J = 1.4 Hz, 1H), 6.58-6.65 (m, 2H), 6.71 (dd, J = 7.8 Hz, J = 1.8 Hz, 1H), 7.11-7.21 (m,10H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 55.5, 64.9, 78.2, 109.6, 111.7, 117.1, 121.0, 126.7, 127.3, 127.7, 128.0, 128.3, 137.1, 140.2, 140.7, 147.4. **HRMS** (ESI): $[M+H]^+$ calcd. 320.1651, found 320.1638.



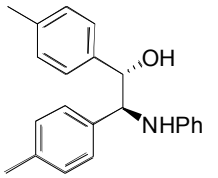
(1*S*,2*S*)-2-(Naphthalen-1-ylamino)-1,2-diphenylethanol (3d). The title compound was isolated as a white solid; melting point: 52-55 °C. The ee was determined by HPLC using a Daicel Chiralcel OD column (19/1 hexane/*i*-PrOH; flow rate 1 mL/min; τ_{minor} = 24.9 min; τ_{major} = 50.3 min); ee

[3] Hou, X.L.; Wu, J.; Dai, L.X.; Xia, L.J.; Tang, M.H. *Tetrahedron: Asymmetry.* **1998**, *9*, 1747.
[4] Schneider, C.; Sreekanth, A.R.; Mai, E. *Angew. Chem. Int. Ed.* **2004**, *43*, 5691.
[5] Bartoli, G.; Bosco, M.; Carlone, A.; Locatelli, M.; Massaccesi, M; Melchiorre, P. Sambri, L. *Org. Lett.* **2004**, *6*, 2173.

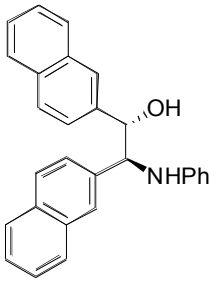
= 91%. $[\alpha]^{22}_D$ = -144.9° (c = 0.390, CH_2Cl_2). **IR** (cm^{-1}): 3401, 3058, 3028, 2923, 1630, 1520, 1051, 831, 745, 700. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 2.72 (br s, 1H), 4.65 (d, *J* = 5.5 Hz, 1H), 4.91 (d, *J* = 6.0 Hz, 1H), 5.51 (br s, 1H), 6.26 (d, *J* = 6.9 Hz, 1H), 7.05-7.28 (m, 12H), 7.39-7.47 (m, 2H), 7.73 (d, *J* = 7.8 Hz, 1H), 7.96 (d, *J* = 7.8 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 64.4, 78.2, 106.6, 117.6, 120.0, 123.9, 124.8, 125.6, 126.4, 126.5, 127.2, 127.5, 127.9, 128.3, 128.5, 128.6, 134.2, 139.9, 140.7, 142.1. **HRMS** (ESI): $[M+H]^+$ calcd. 340.1701, found 340.1698.



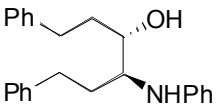
(1*S*,2*S*)-2-(4-Bromo-naphthalen-1-ylamino)-1,2-diphenylethanol (3e). The title compound was isolated as a white solid; melting point: 63-65 °C. The ee was determined by HPLC using a Daicel Chiralcel OD column (9/1 hexane/*i*-PrOH; flow rate 1 mL/min; τ_{minor} = 18 .0 min; τ_{major} = 24.7 min); ee = 86%. $[\alpha]^{22}_D$ = -87.8° (c = 0.435, CH_2Cl_2). **IR** (cm^{-1}): 3423, 3063, 3009, 2923, 1590, 1523, 1475,1380, 1052, 752, 700. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 2.53 (br s, 1H), 4.64 (d, *J* = 5.5 Hz, 1H), 4.98 (d, *J* = 5.0 Hz, 1H), 5.61 (br s, 1H), 6.1 (d, *J* = 8.2 Hz, 1H), 7.19-7.34 (m, 11H), 7.49-7.57 (m, 2H), 7.97 (d, *J* = 8.2 Hz, 1H), 8.15 (dd, *J* = 8.7 Hz, *J* = 1.4 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 64.3, 78.2, 107.2, 110.3, 120.4, 125.2, 125.5, 126.4, 127.0, 127.1, 127.7, 127.8, 128.1, 128.4, 128.6, 130.1, 132.1, 139.5, 140.5, 142.1. **HRMS** (ESI): $[M+H]^+$ calcd. 418.0807, found 418.0793.



(1*S*,2*S*)-2-(phenylamino)-1,2-Di(*p*-tolyl)-ethanol (3f). The title compound was isolated as a white solid; melting point: 41-43°C. The ee was determined by HPLC using a Daicel Chiralpak AD-H column (19/1 hexane/*i*-PrOH; flow rate 1 mL/min; τ_{major} = 26.2 min; τ_{minor} = 31.8 min); ee = 90%. $[\alpha]^{24}_D$ = -47.3° (c = 0.54, CH_2Cl_2). **IR** (cm^{-1}):3400, 3019, 2920, 1602,1503, 1318, 1265, 1050, 820, 749, 691. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 2.24 (s, 3H), 2.27 (s, 3H), 2.75 (br s, 1H), 4.43 (d, *J* = 6.0 Hz, 1H), 4.72 (d, *J* = 6.0 Hz, 1H), 6.48 (d, *J* = 8.2 Hz, 2H), 6.60 (t, *J* = 7.3 Hz, 1H), 6.99-7.12 (m, 10H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ =20.9, 21.0, 64.2, 77.7, 114.0, 117.6, 126.4, 127.1, 128.8, 128.9, 129.1, 136.8, 137.2, 137.3, 137.6, 147.3. **HRMS** (ESI): $[M+H]^+$ calcd. 318.1878, found 318.1900.

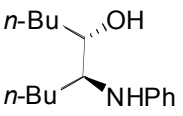


(1*S*,2*S*)-1,2-Di(naphthalen-2-yl)-2-phenylamino-ethanol (3g).[4] The title compound was isolated as a white solid; melting point: 146-148°C. The ee was determined by HPLC using a Daicel Chiralcel OD column (9/1 hexane/*i*-PrOH; flow rate 1 mL/min; τ_{minor} = 38.2 min; τ_{major} = 53.7 min); ee = 91%. $[\alpha]^{22}_D$ = -133.8° (c = 0.410, CH_2Cl_2). **IR** (cm^{-1}): 3399, 3052, 2923, 1601, 1503, 1317, 1265,1051, 819, 749. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 2.90 (br s, 1H), 4.76 (d, *J* = 6.0 Hz, 1H), 5.04 (d, *J* = 5.5 Hz, 1H), 6.52 (d, *J* = 8.7 Hz, 2H), 6.57-6.61 (m, 1H), 6.98-7.02 (m, 2H), 7.28-7.32 (m, 2H), 7.37-7.43 (m, 4H), 7.66-7.76 (m, 8H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 64.6, 76.7, 114.1, 117.9, 124.4, 125.3, 125.6, 125.8, 126.0, 126.1, 126.2, 127.9, 128.0, 128.4, 129.0, 132.9, 133.0, 133.1, 133.3, 137.8, 138.0, 147.2. **HRMS** (ESI): $[M+H]^+$ calcd. 390.1858, found 390.1849.



(3*S*,4*S*)-1,6-Diphenyl-4-phenylamino-hexan-3-ol (3h). The title compound was isolated as a colorless oil. The ee was determined by HPLC

using a Daicel Chiralcel OD column (9/1 hexane/*i*-PrOH; flow rate 0.8 mL/min; τ_{major} = 32.3 min; τ_{minor} = 37.4 min); ee = 60%. $[\alpha]^{22}_D$ = -1.7° (c = 0.525, CH_2Cl_2). **IR** (cm^{-1}): 3047, 3050, 3024, 2926, 2857, 1600, 1497, 1454, 1318, 1060, 748, 698. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 1.74-1.86 (m, 3H), 1.90-1.99 (m, 1H), 2.25 (br s, 1H), 2.56-2.73 (m, 3H), 2.77-2.84 (m, 1H), 3.31-3.34 (m, 1H), 3.61-3.65(m, 1H), 5.57-6.60 (m, 2H), 6.70 (td, J = 7.3 Hz, J = 0.9 Hz, 1H), 6.71-7.29 (m, 12H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 32.2, 32.4, 34.3, 35.8, 57.7, 72.8, 117.6, 125.9, 126.0, 128.4, 128.5, 129.4, 141.6, 141.9, 148.3. **HRMS** (ESI): $[M+H]^+$ calcd. 346.2171, found 346.2182.



(5*S*,6*S*)- 6-Phenylamino-decan-5-ol (3i). The title compound was isolated as a colorless oil. The ee was determined by HPLC using a Daicel Chiralpak AD-H column (19/1 hexane/*i*-PrOH; flow rate 0.8 mL/min; τ_{minor} = 11.7 min; τ_{major} = 12.8 min); ee = 71%. $[\alpha]^{22}_D$ = -2.9° (c = 0.515, CH_2Cl_2). **IR** (cm^{-1}): 3405, 2950, 2951, 2858, 1601, 1457, 747, 692. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.84-0.92 (m, 6H), 1.25-1.65 (m, 12H), 3.23-3.28 (m, 1H), 3.56-3.60 (m, 1H), 6.62-6.70 (m, 3H), 7.13-7.24 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 14.0, 14.1, 22.8, 28.2, 28.4, 32.2, 33.8, 73.5, 113.5, 117.4, 129.3, 148.6. **HRMS** (ESI): $[M+H]^+$ calcd. 250.2171, found 250.2169.