Supporting information
For
Highly Enantioselective Reductive Amination of Simple aryl Ketones
Catalyzed by Ir-f-Binaphane in the Presence of Titanium(IV)
Isopropoxide and Iodine

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General procedure for asymmetric direct reductive amination: In glovebox that was filled with N₂, Aryl ketones (0.5 mmol), *p*-anisidine (74 mg, 0.6 mmol), titanium(IV) isopropoxide (213 mg, 0.75 mmol), and iodine (13 mg, 0.05 mmol) were dissolved in 2 ml DCM. The Ir-(*S,S*)-f-Binaphane complex was made *in situ* by mixing [Ir(COD)Cl]₂ (1.7 mg, 0.0025 mmol) and (*S,S*)-f-Binaphane (4.4 mg, 0.0055 mmol) in 3 ml of DCM. The mixture was stirred for 30 min, and transferred to the substrate solution. This reaction solution was transferred to a Parr bomb. The reductive amination was performed at room temperature under 1000 psi of hydrogen for 10 hours. After the reaction was finished, hydrogen was released carefully and the reaction mixture was passed through a silica gel plug eluted with EtOAc/hexane = 6:1. Solvent was removed under vacuum to yield the product as yellow oil, the yields of all the chiral amines **2a-k** are > 99%. The enantiomeric excess was measured by using HPLC with a chiral column without further purification. The absolute configurations were determined by the sign of the optical rotation.

***R*-(+)-4-Methoxy-*N*-(1-phenyl-ethyl) aniline 2a:** $[\alpha]_D^{25} = +7.0^\circ$ (c = 2, CHCl₃); ¹H-NMR (360 MHz, CDCl₃) δ 1.44 (3H, d, *J* = 6.72 Hz, -CH₃), 3.63 (3H, s, O-CH₃), 3.74 (1H, br., NH), 4.37 (1H, q, *J* = 6.67 Hz, -CH), 6.42-6.45 (2H, m, Ar-H), 6.63-6.68 (2H, m, Ar-H), 7.17-7.20 (1H, m, Ar-H), 7.25-7.33 (4H, m, Ar-H) ppm; ¹³C-NMR (90.6 MHz, CDCl₃) δ 25.3, 54.5, 55.9, 114.8, 115.0, 126.1, 127.0, 128.8, 141.8, 145.7, 152.1 ppm; HRMS (ADCI) calcd. for C₁₅H₁₈NO [M+H]⁺ 228.1388, found 228.1424; 94% ee by HPLC (Chiralcel OD, hexane:2-propanol = 97:3, 1.0 ml/min, *R* isomer *t*₁ = 11.8 min, *S* isomer *t*₂ = 13.2 min).

(+)-*N*-(4-Methoxyphenyl)-1-phenylpropylamine **2b**: $[\alpha]_D^{25} = + 24.6^\circ$ ($c = 2$, CHCl₃); ¹H-NMR (360 MHz, CDCl₃) δ 1.27(3H, t, -CH₃), 2.09-2.18 (2H, m, -CH₂), 4.00 (3H, s, O-CH₃), 4.16 (1H, br., NH), 4.49(1H, t, -CH), 6.78-6.83 (2H, m, Ar-H), 7.00-7.04 (2H, m, Ar-H), 7.52-7.56 (1H, m, Ar-H), 7.61-7.67 (4H, m, Ar-H) ppm; ¹³C-NMR (90.6 MHz, CDCl₃) δ 11.0, 31.8, 55.9, 60.7, 114.6, 114.9, 126.7, 127.0, 128.6, 142.0, 144.3, 152.0 ppm; HRMS (ADCI) calcd. for C₁₆H₂₀NO [M+H]⁺ 242.1545, found 242.1535; 85% ee by HPLC (Chiralcel OD, hexane:2-propanol = 97:3, 1.0 ml/min, (+)- isomer $t_1 = 8.9$ min, (-)- isomer $t_2 = 9.8$ min).

R-(+)-*N*-(4-Methoxyphenyl)-(1-phenyl-pentyl)-amine **2c**: $[\alpha]_D^{25} = + 5.7^\circ$ ($c = 2$, CHCl₃); ¹H-NMR (360 MHz, CDCl₃) δ 1.14 (3H, t, -CH₃), 1.54-1.64(4H, m, CH₂), 1.97-2.06 (2H, m, CH₂), 3.91 (3H, s, O-CH₃), 3.93 (1H, br., NH), 4.47 (1H, t, -CH), 6.69-6.74 (2H, m, Ar-H), 6.91-6.95 (2H, m, Ar-H), 7.43-7.48 (1H, m, Ar-H), 7.52-7.60 (4H, m, Ar-H) ppm; ¹³C-NMR (90.6 MHz, CDCl₃) δ 14.1, 22.8, 28.7, 38.9, 55.9, 59.2, 114.6, 114.9, 126.6, 126.9, 128.6, 142.0, 144.8, 152.0 ppm; HRMS (ADCI) calcd. for C₁₈H₂₄NO [M+H]⁺ 270.1858, found 270.1843; 79% ee by HPLC (Chiralcel OD, hexane:2-propanol = 97:3, 1.0 ml/min, *R* isomer $t_1 = 7.7$ min, *S* isomer $t_2 = 8.3$ min).

(+)-*N*-(4-Methoxyphenyl)-(1-*o*-tolyl-ethyl)-amine **2d**: $[\alpha]_D^{25} = + 9.2^\circ$ ($c = 2$, CHCl₃); ¹H-NMR (360 MHz, CDCl₃) δ 1.67 (3H, d, $J = 6.60$ Hz, -CH₃), 2.66 (3H, s, Ar-CH₃), 3.90 (3H, s, O-CH₃), 3.91 (1H, br., NH), 4.83 (1H, q, $J = 6.53$ Hz, -CH), 6.62-6.65 (2H, m, Ar-H), 6.89-6.93 (2H, m, Ar-H), 7.35-7.41 (3H, m, Ar-H), 7.64-7.66 (1H, m, Ar-H) ppm; ¹³C-NMR (90.6 MHz, CDCl₃) δ 19.1, 23.2, 50.6, 55.8, 114.4, 115.0, 124.8, 126.7, 130.7, 134.7, 141.7, 143.1, 152.0 ppm; HRMS (ADCI) calcd. for C₁₆H₂₀NO [M+H]⁺ 242.1545, found 242.1555; 44% ee by HPLC (Chiralcel OD, hexane:2-propanol = 97:3, 1.0 ml/min, (+)-isomer $t_1 = 9.1$ min, (-)- isomer $t_2 = 11.8$ min).

(+)-*N*-(4-Methoxyphenyl)-(1-*m*-tolyl-ethyl)-amine **2e**: $[\alpha]_D^{25} = + 8.1^\circ$ ($c = 2$, CHCl₃); ¹H-NMR (360 MHz, CDCl₃) δ 1.82 (3H, d, $J = 6.67$ Hz, -CH₃), 2.68(3H, s, Ar-CH₃), 4.02 (3H, s, O-CH₃), 4.04 (1H, br., NH), 4.72 (1H, q, $J = 6.65$ Hz, -CH), 6.81-6.84 (2H, m, Ar-H), 7.03-7.06 (2H, m, Ar-H), 7.37-7.39 (1H, m, Ar-H), 7.50-7.57(3H, m, Ar-H) ppm; ¹³C-NMR (90.6 MHz, CDCl₃) δ 21.6, 25.2, 54.4, 55.8, 114.7, 114.9, 123.1, 126.7, 127.7, 128.6, 138.2, 141.9, 145.7, 152.0 ppm; HRMS (ADCI) calcd. for C₁₆H₂₀NO

[M+H]⁺ 242.1545, found 242.1544; 89% ee by HPLC (Chiralcel OD, hexane:2-propanol = 97:3, 1.0 ml/min, (+)-isomer t_1 = 10.0 min, (-)- isomer t_2 = 11.5 min).

(+)-N-(4-Methoxyphenyl)-(1-*p*-tolyl-ethyl)-amine 2f: $[\alpha]_D^{25} = +10.7^\circ$ (c = 2, CHCl₃); ¹H-NMR (360 MHz, CDCl₃) δ 1.76 (3H, d, J = 6.69 Hz, -CH₃), 2.61(3H, s, Ar-CH₃), 3.96 (3H, s, O-CH₃), 3.97 (1H, br., NH), 4.68(1H, q, J = 6.63 Hz, -CH), 6.75-6.79 (2H, m, Ar-H), 6.97-7.01 (2H, m, Ar-H), 7.40-7.45 (2H, m, Ar-H), 7.53-7.55(2H, m, Ar-H) ppm; ¹³C-NMR (90.6 MHz, CDCl₃) δ 21.2, 25.2, 54.0, 55.8, 114.9, 125.9, 129.4, 136.4, 141.8, 142.6, 152.0 ppm; HRMS (ADCI) calcd. for C₁₆H₂₀NO [M+H]⁺ 242.1545, found 242.1550; 96% ee by HPLC (Chiralcel OD, hexane:2-propanol = 97:3, 1.0 ml/min, (+)-isomer t_1 = 9.8 min, (-)- isomer t_2 = 11.2 min).

(+)-N-(4-Methoxyphenyl)-{1-(*p*-methoxy-phenyl)-ethyl}-amine 2g: $[\alpha]_D^{25} = +23.8^\circ$ (c = 2, CHCl₃); ¹H-NMR (360 MHz, CDCl₃) δ 1.78 (3H, d, J = 6.67 Hz, -CH₃), 3.99(3H, s, O-CH₃), 4.03 (1H, br., NH), 4.07 (3H, s, O-CH₃), 4.69(1H, q, J = 6.61 Hz, -CH), 6.78-6.81 (2H, m, Ar-H), 7.00-7.03 (2H, m, Ar-H), 7.15-7.23 (2H, m, Ar-H), 7.59(2H, d, J = 8.65 Hz, Ar-H) ppm; ¹³C-NMR (90.6 MHz, CDCl₃) δ 25.1, 53.7, 55.3, 55.8, 114.1, 114.7, 114.9, 127.0, 137.6, 141.8, 152.0, 158.6 ppm; HRMS (ADCI) calcd. for C₁₆H₂₀NO₂ [M+H]⁺ 258.1494, found 258.1498; 95% ee by HPLC (Chiralcel OD, hexane:2-propanol = 97:3, 1.0 ml/min, (+)-isomer t_1 = 14.5 min, (-)- isomer t_2 = 16.3 min).

(-)-N-(4-Methoxyphenyl)-{1-(*p*-fluoro-phenyl)-ethyl}-amine 2h: $[\alpha]_D^{25} = -6.7^\circ$ (c = 2, CHCl₃); ¹H-NMR (360 MHz, CDCl₃) δ 1.73 (3H, d, J = 6.66 Hz, -CH₃), 3.90 (1H, br., NH), 3.96 (3H, s, O-CH₃), 4.66 (1H, q, J = 6.62 Hz, -CH), 6.71-6.74 (2H, m, Ar-H), 6.97-6.99 (2H, m, Ar-H), 7.24-7.29 (2H, m, Ar-H), 7.57-7.61 (2H, m, Ar-H) ppm; ¹³C-NMR (90.6 MHz, CDCl₃) δ 25.3, 53.8, 55.8, 114.9, 115.4, 115.6, 127.5, 127.6, 141.3, 141.4, 141.5, 152.2, 160.5, 163.2 ppm; HRMS (ADCI) calcd. for C₁₅H₁₇NOF [M+H]⁺ 246.1294, found 246.1296; 93% ee by HPLC (Chiralcel OD, hexane:2-propanol = 97:3, 1.0 ml/min, (-)- isomer t_1 = 14.2 min, (+)- isomer t_2 = 16.5 min).

(+)-N-(4-Methoxyphenyl)-{1-(*p*-chloro-phenyl)-ethyl}-amine 2i: $[\alpha]_D^{25} = +23.1^\circ$ (c = 2, CHCl₃); ¹H-NMR (360 MHz, CDCl₃) δ 1.55 (3H, d, J = 6.71 Hz, -CH₃), 3.78 (3H, s, O-CH₃), 3.82 (1H, br., NH), 4.47 (1H, q, J = 6.69 Hz, -CH), 6.53-6.56 (2H, m, Ar-H), 6.79-6.82 (2H, m, Ar-H), 7.35-7.40 (4H, m, Ar-H) ppm; ¹³C-NMR (90.6 MHz, CDCl₃) δ 25.2, 53.8, 55.8, 114.9, 127.4, 128.9, 132.4, 141.4, 144.2, 152.2 ppm; HRMS (ADCI)

calcd. for $C_{15}H_{17}NOCl$ $[M+H]^+$ 262.0999, found 262.0990; 92% ee by HPLC (Chiralcel OD, hexane:2-propanol = 97:3, 1.0 ml/min, (+)- isomer t_1 = 15.4 min, (-)- isomer t_2 = 18.7 min).

(+)-*N*-(4-Methoxyphenyl)-{1-(*p*-bromo-phenyl)-ethyl}-amine 2j: $[\alpha]^{25}_D = +28.4^\circ$ ($c = 2$, $CHCl_3$); 1H -NMR (360 MHz, $CDCl_3$) δ 1.52 (3H, d, $J = 6.72$ Hz, $-CH_3$), 3.75 (3H, s, O- CH_3), 3.78 (1H, br., NH), 4.42 (1H, q, $J = 6.67$ Hz, $-CH$), 6.48-6.53 (2H, m, Ar-H), 6.75-6.79 (2H, m, Ar-H), 7.27-7.31 (2H, m, Ar-H), 7.47-7.51 (2H, m, Ar-H) ppm; ^{13}C -NMR (90.6 MHz, $CDCl_3$) δ 25.2, 53.9, 55.8, 114.7, 114.9, 120.5, 127.8, 131.8, 141.3, 144.8, 152.2 ppm; HRMS (ADCI) calcd. for $C_{15}H_{17}NOBr$ $[M+H]^+$ 306.0494, found 306.0505; 94% ee by HPLC (Chiralcel OD, hexane:2-propanol = 97:3, 1.0 ml/min, (+)- isomer t_1 = 16.5 min, (-)- isomer t_2 = 20.2 min).

(+)-*N*-(4-Methoxyphenyl)-{1-(2'-furan)-ethyl}-amine 2k: $[\alpha]^{25}_D = +92.9^\circ$ ($c = 2$, $CHCl_3$); 1H -NMR (360 MHz, $CDCl_3$) δ 1.79 (3H, d, $J = 6.72$ Hz, $-CH_3$), 3.80 (1H, br., NH), 3.98 (3H, s, O- CH_3), 4.81 (1H, q, $J = 6.71$ Hz, $-CH$), 6.39-6.40 (1H, m, Ar-H), 6.53-6.54 (1H, m, Ar-H), 6.83-6.88 (2H, m, Ar-H), 6.99-7.04 (2H, m, Ar-H), 7.58-7.59 (1H, m, Ar-H) ppm; ^{13}C -NMR (90.6 MHz, $CDCl_3$) δ 21.1, 48.5, 55.8, 105.1, 105.3, 110.1, 110.3, 114.9, 115.3, 141.3, 141.5, 152.6, 157.7 ppm; HRMS (ADCI) calcd. for $C_{13}H_{16}NO_2$ $[M+H]^+$ 218.1181, found 218.1212; 92% ee by HPLC (Chiralpak OJ, hexane:2-propanol = 80:20, 1.0 ml/min, (-)- isomer t_1 = 12.6 min, (+)- isomer t_2 = 16.1 min).

Procedure for oxidation deprotection of chiral amine 2a: The chiral amine, *R*-(+)-4-Methoxy-*N*-(1-phenyl-ethyl) aniline **2a** (85 mg, 0.395 mmol, 93.3% ee) was dissolved into a mixture of MeOH/ H_2O (20 ml, 4:1), after the reaction solution was cooled to 0 °C, CAN (cerium ammonium nitrate) (866 mg, 1.58 mmol) was added in one portion, the resulting reaction system was stirred for 6 hours at the same temperature. Water was added and the solution was washed with CH_2Cl_2 . The aqueous solution was made alkaline by adding 1N NaOH, and then extracted with ethyl acetate. The combined organic solution was washed with brine and dried over Na_2SO_4 . The solvent was removed under vacuum, and the residue was purified through silica gel column chromatography,

eluted with ethyl acetate, to afford the chiral primary amine **5** as yellow oil (39 mg, 81.3% yield).

R-(+)- α -Methyl-benzylamine 5: $[\alpha]_D^{25} = +29.9^\circ$ (c = 1, CHCl₃); ¹H-NMR (360 MHz, CDCl₃) δ 1.55 (3H, d, J = 6.59 Hz, -CH₃), 1.63 (2H, br., NH₂), 4.27 (1H, q, J = 6.57 Hz, -CH), 7.39-7.42(1H, m, Ar-H), 7.47-7.53 (4H, m, Ar-H) ppm; ¹³C-NMR (90.6 MHz, CDCl₃) δ 25.6, 51.1, 125.5, 126.6, 128.3, 147.7 ppm. 95% ee by GC after protection with acetic anhydride (Chiralselect 1000, dimension 30 m 0.25 mm, column temperature 160 °C, carrier gas: He (1 ml/min), *S*- isomer t_1 = 18.7 min, *R*- isomer t_2 = 19.7 min).