Supporting Information

Palladium-Catalyzed Asymmetric Hydrogenation of Functionalized Ketones

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General. NMR spectra were recorded on Bruker-DRX 400 spectrometers. The chemical shifts were reported in ppm downfield from tetramethylsilane (TMS) with the solvent resonance as the internal standard. Coupling constants ($J$) are reported in Hz and refer to apparent peak multiplications. Optical rotations were measured with JASCO P-1010 polarimeter. Flash column chromatography was performed on silica gel (200-300 mesh). TLC analysis was performed using glass-backed plates coated with 0.2 mm silica.

Commerciially available reagents were used throughout without further purification other than those detailed below. THF, Et₂O and benzene were distilled over sodium benzophenone ketyl under nitrogen. Methylene chloride and 1,2-Dichloroethane were distilled over calcium hydride. CF₃CH₂OH and acetone were stilled from anhydrous CaSO₄. MeOH, EtOH and i-ProOH were purchased from Aldrich without purification. Ketone 5 was distilled under nitrogen before use. (S)-SYNPHOS was prepared according to the literature. All reactions were carried out under an atmosphere of nitrogen using standard Schlenk techniques or in a nitrogen-filled glovebox, unless otherwise noted.

General procedure for the synthesis of phthalimide ketones:

In a dried flask, to a stirred solution of phthalimide (5.05 mmol) in DMF (10mL) was added potassium carbonate (6 mmol) at room temperature (the reaction can be carried out in the air without special handling). After being stirred for 30 mintues, α-bromide-ketone (5 mmol) was added and the stirring was continued at room temperature for 1.5~4h (monitored by TLC). After the reaction was complete, the reaction mixture was poured into water (100 mL). The desired products yield can be collected via filtration which normally is good enough for asymmetric hydrogenation as substrates. Further purification can be obtained via recrystalization from ethanol or petro-ether/CH₂Cl₂.

2-Phthalimide-1-phenylethanone (1a): White solid, $^1$H NMR (400 MHz, CDCl₃): $\delta$ = 5.14 (s, 2H), 7.52 (t, $J$ = 7.6 Hz, 2H), 7.64 (t, $J$ = 7.4 Hz, 1H), 7.74-7.77 (m, 2H), 7.89-7.92 (m, 2H).

2-Phthalimide-1-(4-fluoro-phenyl)-ethanone (1b): White solid, $^1$H NMR (400 MHz, CDCl₃): $\delta$ = 5.10 (s, 2H), 7.20 (t, $J$ = 8.4 Hz, 2H), 7.76 (dd, $J$ = 3.2, 5.2 Hz, 2H), 7.89-7.92 (m, 2H), 8.05 (dd, $J$ = 5.4, 8.6 Hz, 2H).

2-Phthalimide-1-(4-methoxy-phenyl)-ethanone (1e): White solid, $^1$H NMR (400 MHz, CDCl₃): $\delta$ = 5.10 (s, 2H), 7.31 (d, $J$ = 4.8 Hz, 2H), 7.34-7.37 (m, 2H), 7.47-7.50 (m, 3H), 7.64-7.66 (m, 2H), 7.73-7.76 (m, 4H), 8.09 (d, $J$ = 8.0 Hz, 2H).
CDCl$_3$): $\delta$ = 3.89 (s, 3H), 5.09 (s, 2H), 6.98 (d, $J = 8.0$ Hz, 2H), 7.74-7.77 (m, 2H), 7.88-7.91 (m, 2H), 7.99 (d, $J = 8.0$ Hz, 2H).

2-Phthalimide-1-(3-methoxy-phenyl)-ethanone (1f): White solid, $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 3.86 (s, 3H), 5.12 (s, 2H), 7.18 (q, $J = 4.0$ Hz, 1H), 7.43 (t, $J = 8.0$ Hz, 1H), 7.51 (s, 1H), 7.60 (d, $J = 8.0$ Hz, 1H), 7.75-7.77 (m, 2H), 7.89-7.91 (m, 2H).

2-Phthalimide-1-(2-methoxy-phenyl)-ethanone (1g): White solid, $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 4.01 (s, 3H), 5.09 (s, 2H), 7.05 (t, $J = 8.0$ Hz, 2H), 7.54 (t, $J = 4.0$ Hz, 1H), 7.73-7.75 (m, 2H), 7.89-7.95 (m, 3H).

2-Phthalimide-1-naphthalen-2-yl-ethanone (1h): White solid, $^1$H NMR (400 MHz, DMSO): $\delta$ = 5.40 (s, 2H), 7.71 (dd, $J = 7.6$, 14.0 Hz, 2H), 7.92-8.19 (m, 8H), 8.92 (s, 1H).

1-Phthalimide-3,3-dimethyl-butan-2-one (1j): White solid, $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 1.29 (d, $J = 8.0$ Hz, 9H), 4.64 (s, 2H), 7.72-7.79 (m, 2H), 7.85-7.88 (m, 2H).

2-Phthalimide-1-(4-bromo-phenyl)-ethanone (1k): White solid, $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 5.09 (s, 2H), 7.67 (dd, $J = 8.4$ Hz, 2H), 7.76-7.79 (m, 2H), 7.89-7.95 (m, 3H).

α-Benzamidoacetophenone (3): It was prepared according to the literature. White solid, $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 4.98 (d, $J = 4.4$ Hz, 2H), 7.32 (br, 1H), 7.46-7.56 (m, 5H), 7.64-7.68 (m, 1H), 7.90 (d, $J = 8.0$ Hz, 2H), 8.05 (d, $J = 8.0$ Hz, 2H).

Preparation of complex PdCl$_2$-(S)-SYNPHOS: PdCl$_2$(CH$_3$CN)$_2$ (77.8 mg, 0.3 mmol) was suspended in 5 mL of benzene. (S)-SYNPHOS (287 mg, 0.45 mmol) was added and the mixture was stirred at room temperature. The yellow precipitate was collected by filtration and washed with Et$_2$O, and dried in vacuo: yield of [Pd((S)-SYNPHOS)]$[\text{Cl}]_2$ 242 mg (99%).

Preparation of complex Pd(OTf)$_2$-(S)-SYNPHOS: The orange powder [Pd((S)-SYNPHOS)][Cl]$_2$ (0.210 g, 0.257 mmol) was placed into a Schlenk flask equipped with a stirbar and dissolved in CH$_2$Cl$_2$ (16 mL). Then, 0.159 g (0.620 mmol) of AgOTf was added, and the resulting solution was stirred under nitrogen for 20 h at room temperature. The precipitate was filtered, and the filtrate was reduced in volume to about 3 mL in vacuo. Then 5 ul (0.334 mmol) of distilled water was added, followed by the addition 12 mL of Et$_2$O. The yellow precipitate was collected by filtration and washed with Et$_2$O and was dried in vacuo: yield of [Pd((S)-SYNPHOS)(H$_2$O)][OTf]$_2$ 254 mg (93%).

General procedure for asymmetric hydrogenation: Ligand (0.006 mmol) and Pd(CF$_3$CO$_2$)$_2$ (1.7 mg, 0.005 mmol) were placed in a dried Schlenk tube under a nitrogen atmosphere, and degassed anhydrous acetone was added. The mixture was stirred at room temperature for about 1 h. The solvent was removed under vacuum to give the catalyst (Pure complex was directly used as the catalyst). This catalyst was taken into a glove box filled with nitrogen and dissolved in dry TFE (1-3 mL). To the substrates (0.25 mmol) was added this catalyst solution, and then the mixture was transferred to a autoclave. The autoclave was stirred under the desired conditions. The hydrogen was carefully released. The solvents were removed. Conversion was directly determined by $^1$H NMR spectroscopy. The enantiomeric excess was determined by HPLC after purification on silica gel or by GC. The absolute configuration of was determined by measurement of its optical rotation and comparison to the literature value.

2-Phthalimide-1-phenyl-ethanol (2a): White solid, 91.7% $ee$ (R), $[\alpha]_D^{21}$ = -22.1 ($c$ 1.07, CHCl$_3$). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 2.85 (br, 1H), 3.93-4.06 (m, 2H), 5.06-5.09 (m, 2H), 7.29-7.47 (m, 5H), 7.72-7.75 (m, 2H), 7.85-7.87 (m, 2H); HPLC (Chiralcel OJ-H column, iPrOH/hexane 20/80, 1.0 mL min$^{-1}$, 254nm): $t_1 = 18.6$ min (R), $t_2 = 26.1$ min (S).
2-Phthalimide-1-(4-fluoro-phenyl)-ethanol (2b): White solid, 92.2% ee (R), [α]$_D^{21} = -17.0$ (c 1.15, CHCl$_3$); ¹H NMR (400 MHz, CDCl$_3$): δ = 2.94 (br, 1H), 3.83-3.96 (m, 2H), 4.99 (q, J = 4.0 Hz, 1H), 6.95-6.99 (m, 2H), 7.33-7.37 (m, 2H), 7.66 (dd, J = 3.0, 5.4 Hz, 2H), 7.78 (dd, J = 3.2, 5.6 Hz, 2H); HPLC (Chiralcel OJ-H column, iPrOH/hexane 40/60, 1.0 mL min$^{-1}$, 254nm): t$_1$ = 8.1 min (R), t$_2$ = 11.2 min (S).

2-Phthalimide-1-p-tolyl-ethanol (2c): White solid, 92.2% ee (R), [α]$_D^{21} = -22.2$ (c 1.09, CHCl$_3$); ¹H NMR (400 MHz, CDCl$_3$): δ = 2.34 (s, 3H), 2.75 (br, 1H), 3.90-4.04 (m, 2H), 5.01-5.06 (m, 1H), 7.18 (d, J = 7.6 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 7.72-7.74 (m, 2H), 8.74-8.78 (m, 2H); HPLC (Chiralcel OJ-H column, iPrOH/hexane 40/60, 1.0 mL min$^{-1}$, 254nm): t$_1$ = 14.6 min (R), t$_2$ = 18.2 min (S).

2-Phthalimide-1-biphenyl-4-yl-ethanol (2d): White solid, 92.0% ee (R), [α]$_D^{16} = -14.0$ (c 1.00, CHCl$_3$); ¹H NMR (400 MHz, DMSO): δ = 3.67 (dd, J = 4.6, 13.8, 1H), 3.79 (dd, J = 8.8, 13.6 Hz, 1H), 4.96 (q, J = 4.4 Hz, 1H), 5.70 (br, 1H), 7.36 (t, J = 7.4 Hz, 1H), 7.47 (d, J = 8.0 Hz, 4H), 7.64-7.66 (m, 4H), 7.83-7.90 (m, 4H); 13C NMR (100 MHz, DMSO): δ = 45.5, 69.3, 123.0, 126.6, 127.4, 129.0, 131.7, 134.4, 139.2, 139.9, 141.7, 167.9; HPLC (Chiralcel OJ-H column, iPrOH/hexane 40/60, 1.0 mL min$^{-1}$, 254nm): t$_1$ = 15.6 min (R), t$_2$ = 19.7 min (S).

2-Phthalimide-1-(4-methoxy-phenyl)-ethanol (2e): White solid, 75.2% ee (S), [α]$_D^{17} = +16.9$ (c 1.00, CHCl$_3$); ¹H NMR (400 MHz, CDCl$_3$): δ = 2.72 (br, 1H), 3.80 (d, J = 2.4 Hz, 3H), 3.89-4.04 (m, 2H), 5.02 (q, J = 4.3 Hz, 1H), 6.89 (dd, J = 2.2, 9.0 Hz, 2H), 7.36-7.39 (m, 2H), 7.72-7.74 (m, 2H), 7.84-7.87 (m, 2H); HPLC (Chiralcel OJ-H column, iPrOH/hexane 40/60, 1.0 mL min$^{-1}$, 254nm): t$_1$ = 15.2 min (R), t$_2$ = 20.9 min (S).

2-Phthalimide-1-(3-methoxy-phenyl)-ethanol (2f): White solid, 92.0% ee (R), [α]$_D^{13} = -21.8$ (c 1.00, CHCl$_3$); ¹H NMR (400 MHz, CDCl$_3$): δ = 2.93 (br, 1H), 3.81 (s, 3H), 3.91-4.05 (m, 2H), 5.02-5.07 (m, 1H), 6.83-6.85 (m, 1H), 7.02 (d, J = 7.6 Hz, 2H), 7.28-7.30 (m, 1H), 7.73 (dd, J = 3.0, 5.4 Hz, 2H), 7.85 (dd, J = 3.0, 5.4 Hz, 2H); HPLC (Chiralcel OJ-H column, iPrOH/hexane 40/60, 1.0 mL min$^{-1}$, 254nm): t$_1$ = 15.0 min (R), t$_2$ = 16.8 min (S).

2-Phthalimide-1-(2-methoxy-phenyl)-ethanol (2g): White solid, 80.4% ee (R), [α]$_D^{16} = -30.62$ (c 0.97, CHCl$_3$); ¹H NMR (400 MHz, CDCl$_3$): δ = 3.43 (br, 1H), 3.90 (s, 3H), 3.98 (dd, J = 4.0, 14.0 Hz, 1H), 4.16 (dd, J = 8.4, 13.6 Hz, 1H), 5.14 (s, 1H), 6.88-6.95 (m, 2H), 7.26 (dd, J = 1.4, 15.4 Hz, 1H), 7.35 (d, J = 7.6 Hz, 1H), 7.69-7.71 (m, 2H), 7.80-7.83 (m, 2H); HPLC (Chiralcel OJ-H column, iPrOH/hexane 20/80, 1.0 mL min$^{-1}$, 254nm): t$_1$ = 15.0 min (R), t$_2$ = 16.8 min (S).

2-Phthalimide-1-naphthalen-2-yl-ethanol (2h): White solid, 88.8% ee (R), [α]$_D^{16} = -19.2$ (c 0.51, CHCl$_3$); ¹H NMR (400 MHz, CDCl$_3$): δ = 3.05 (br, 1H), 4.01-4.14 (m, 2H), 5.24 (t, J = 4.2 Hz, 1H), 7.48 (dd, J = 4.0, 5.6 Hz, 2H), 7.59 (s, 1H), 7.71-7.73 (m, 2H), 7.82-7.87 (m, 5H), 7.93 (s, 1H); 13C NMR (100 MHz, CDCl$_3$): δ = 46.3, 73.4, 124.1, 124.3, 125.5, 126.7, 126.8, 128.3, 128.6, 129.0, 132.4, 133.8, 134.7, 139.0, 169.4; HPLC (Chiralcel OJ-H column, iPrOH/hexane 40/60, 1.0 mL min$^{-1}$, 254nm): t$_1$ = 13.1 min (R), t$_2$ = 19.5 min (S).

1-Phthalimide-propan-2-ol (2i): White solid, 89.8% ee (R), [α]$_D^{16} = -22.0$ (c 1.02, CHCl$_3$); ¹H NMR (400 MHz, CDCl$_3$): δ = 1.27 (d, J = 6.4 Hz, 3H), 2.32 (br, 1H), 3.70-3.81 (m, 2H), 4.10-4.15 (m, 1H) 7.71-7.76 (m, 2H), 7.84-7.89 (m, 2H); HPLC (Chiralcel OJ-H column, iPrOH/hexane 15/85, 1.0 mL min$^{-1}$, 254nm): t$_1$ = 20.0 min (R), t$_2$ = 21.9 min (S).

1-Phthalimide-3,3-dimethyl-butan-2-ol (2j): Oil or solid, 88.0% ee (R), [α]$_D^{13} = -29.8$ (c 1.10, CHCl$_3$); ¹H NMR (400 MHz, CDCl$_3$): δ = 1.02 (d, J = 5.2 Hz, 9H), 2.27 (br, 1H), 3.51-3.55 (m, 1H), 3.67 (dd, J = 10.0, 14.0 Hz, 1H), 3.94 (dd, J = 2.0, 14.0 Hz, 1H), 7.71-7.73 (m, 2H), 7.83-7.86 (m,
2H) ; HPLC (Chiralcel OJ-H column, iPrOH/hexane 40/60, 1.0 mL min⁻¹, 254nm): t₁ = 5.3 min (R), t₂ = 6.5 min (S).

**2-Benzamido-1-Phenylethanol (6):** White solid, 74.6% ee (R), [α]⁺¹⁶ D = -56.5 (c 0.75, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ = 3.26 (br, 2H), 3.51-3.57 (m, 1H), 3.91-3.97 (m, 1H), 4.96-5.00 (m, 1H), 6.58 (br, 1H), 7.30-7.54 (m, 8H), 7.76 (d, J = 7.6 Hz, 2H); HPLC (Chiralcel OJ-H column, iPrOH/hexane 10/90, 1.0 mL min⁻¹, 254nm): t₁ = 10.5 min (R), t₂ = 12.0 min (S).

**Ethyl 3-Hydroxy-3-phenyl-propanoate (7):** Light yellow oil, ¹H NMR (400 MHz, CDCl₃): δ = 1.26 (t, J = 7.2 Hz, 3H), 2.68-2.79 (m, 2H), 3.30 (br, 1H), 4.18 (q, J = 7.2 Hz, 2H), 5.13 (dd, J = 4.0, 8.8 Hz, 1H), 7.27-7.39 (m, 5H); HPLC (Chiralcel OD-H column, iPrOH/hexane 20/80, 0.5 mL min⁻¹, 254nm): t₁ = 10.9 min (S), t₂ = 13.3 min (R).

**1-Phenylethanol (8):** GC (β-120, 120°C isothermal): 16.3 min (R), 17.2 min (S).

**Reference**