Synthesis of Novel Chiral Benzophospholanes and Their Application in Asymmetric Hydrogenation

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Supporting Information

General Remarks:

All melting points were measured on a Yanaco MP-500D melting point apparatus. Optical rotations were measured on a JASCO DIP-4. ^{1}H NMR and ^{31}P NMR spectra were obtained on a Bruker DRX500 spectrometer (^{1}H: 500 MHz, ^{31}P: 202 MHz), and mass spectra were measured on a HITACHI M-80B mass spectrometer. All reactions were performed under a nitrogen atmosphere.

Ethyl 4-(2-fluorophenyl)-2-methyl-3-oxobutyrate (4)

1,1'-Carbonylbis-1*H*-imidazole (23.0 g, 142 mmol) was added to a solution of 2-fluorophenylacetic acid (20.0 g, 129 mmol) in acetonitrile (30 mL) at room temperature. After stirring for 1 h, the resultant solution was added to a mixture of ethyl potassium methylmalonate (33.3 g, 181 mmol), magnesium chloride (14.7 g, 155 mmol) and acetonitrile (60 mL). The mixture was stirred overnight at 45 °C, then treated with 1 N HCl (200 mL) and extracted 3 times with ethyl acetate (200 mL). The combined organic layer was washed with 1 N HCl, 5% sodium carbonate solution, water and brine and then dried over Na_2SO_4 followed by evaporation *in vacuo*. Purification of the residue using silica gel column chromatography gave **4** (23.1 g, 95% yield).

^{1}H NMR ($CDCl_3$): δ 1.27 (3H, t, *J* = 7.2 Hz), 1.36 (3H, d, *J* = 7.2 Hz), 3.64 (1H, q, *J* = 7.2 Hz), 3.88 (2H, s), 4.18 (2H, q, *J* = 7.2 Hz), 6.95–7.15 (4H, m); EI-MS: *m/z* 238 $(M)^+$

Ethyl 4-(2-fluorophenyl)-3-hydroxy-2-methylbutyrate (5)

A 500 mL stainless steel autoclave was charged under a nitrogen stream with [{RuCl((*R*)-segphos)}$_2$(μ-Cl)$_3$][Me_2NH_2] (138 mg, 0.084 mmol), **4** (20 g, 83.9 mmol) and ethanol (80 mL). Hydrogen (3.0 MPa) was introduced and the mixture was stirred for 18 h at 80 °C. Evaporation *in vacuo* and purification by silica gel chromatography gave **5** as a diastereo mixture (*ca.* 1:1) (18.6 g, 93% yield). The optical purity of the two diastereomers was 96.9% ee and 98.5% ee, respectively. The optical purity was determined by GC analysis (Cp Chirasil DEX-CB).

EI-MS: *m/z* 241 $(M+1)^+$

4-(2-fluorophenyl)-2-methylbutane-1,3-diol

A solution of **5** (18.0g, 74.9 mmol) in THF (180 mL) was added to a suspension of lithium aluminium hydride (2.84 g, 74.9 mmol) in THF (30 mL). The reaction mixture was stirred for 18 h at room temperature, and water (5 mL) and 1 N NaOH (5 mL) were added. Filtration, evaporation *in vacuo* and purification by silica gel chromatography gave the product (14.5 g, 99% yield).

EI-MS: *m/z* 199 $(M+1)^+$

4-(2-Fluorophenyl)-3-hydroxy-2-methylbutyl *p*-toluenesulfonate

4-(2-Fluorophenyl)-2-methylbutane-1,3-diol (13.5 g, 68.1 mmol), triethylamine (14.2 mL, 21.3 mmol), dichloromethane (70 mL) was cooled to 0 °C and *p*-toluenesulfonyl chloride (13.0 g, 68.1 mmol) was added. After stirring overnight at room temperature, the reaction mixture was treated with water and extracted 3 times with dichloromethane. The combined extract was dried over Na_2SO_4 and evaporated *in vacuo*. Purification of the residue by silica gel column chromatography gave the product (21.1 g, 88% yield).

EI-MS: *m/z* 353 $(M+1)^+$

(+)-1-(2-Fluorophenyl)-3-methylbutan-2-ol ((+)-6)

A solution of 4-(2-fluorophenyl)-3-hydroxy-2-methylbutyl *p*-toluenesulfonate (21.1 g, 60.2 mmol) in THF (210 mL) was added into a suspension of lithium aluminium hydride (2.28 g) in THF (25 mL) at room temperature. The reaction mixture was stirred for 30 min, followed by the addition of $Na_2SO_4 \bullet 10H_2O$. Filtration, evaporation *in vacuo* and purification by silica gel chromatography gave (+)-**6** (9.6 g, 88% yield, 98.1% ee). The ee was determined by GC analysis (Cp Chirasil DEX-CB).

Mp: 37–38 °C; $[\alpha]_D^{24}$: +27.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.01 (6H, d, *J* = 6.6 Hz), 1.76 (1H, dqq, *J* = 5.5, 6.6, 6.6 Hz), 2.63 (1H, dd, *J* = 9.63, 13.2 Hz), 2.92 (1H, dd, *J* = 2.7, 13.2 Hz), 3.64 (1H, m), 7.00–7.10 (2H, m), 7.18–7.28 (2H, m); EI-MS: *m/z* 182 $(M)^+$

(+)-1-(2-Fluorobenzyl)-2-methylpropyl methanesulfonate ((+)-7)

A mixture of **6** (8.6 g, 47.2 mmol), triethylamine (7.9 mL, 56.6 mmol) and dichloromethane (40 mL) was cooled to 0 °C, and then methanesulfonyl chloride (4.0 mL, 51.9 mmol) was added to the mixture. The reaction mixture was stirred overnight at room temperature, then treated with water and extracted 3 times with dichloromethane. The combined extract was washed with brine, dried over Na_2SO_4 and evaporated *in vacuo*. Purification by silica gel column chromatography gave (+)-**7** (12.5 g, 91% yield).

$[\alpha]_D^{24}$: +30.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.06 (3H, d, *J* = 7.0 Hz), 1.08 (3H, d, *J* = 7.0 Hz), 2.07 (1H, dqq, *J* = 4.2, 7.0, 7.0 Hz), 2.48 (3H, s), 2.93 (1H, dd, *J* = 9.0, 14.6 Hz), 3.06 (1H, dd, *J* = 4.4, 14.6 Hz), 4.77 (1H, ddd, *J* = 4.2, 4.4, 9.0 Hz), 6.98–7.15 (2H, m), 7.18–7.32 (2H, m)

(+)-1,2-Bis(2-isopropyl-2,3-dihydro-1*H*-phosphindol-1-yl)benzene ((+)-iPr-BeePHOS) ((+)-2b)

1,2-Bis(phosphino)benzene (300 μl, 2.32 mmol) in THF (9 mL) was cooled to 0 °C and 1.6M *n*-butyllithium in hexane (2.9 mL, 4.64 mmol) was added dropwise. After stirring 1 h at 0 °C, a solution of (+)-**7** (1.21 g, 4.64 mmol) in THF (12 mL) was added. The reaction mixture was stirred for 1 h at 0 °C and then for 1 h at room temperature. The mixture was cooled to 0 °C and 1.6 M *n*-butyllithium in hexane (4.4 mL, 6.96 mmol) was added. Subsequently it was stirred overnight at room temperature. The reaction mixture was treated with water (1 mL) and evaporated *in vacuo*. The residue was then treated with water and extracted 3 times with diethyl ether. The combined extract was washed with water and evaporated *in vacuo*. Purification by silica gel column chromatography gave (+)-**2b** (227 mg, 23% yield).

Mp: 70–71 °C; $[\alpha]_D^{24}$: +186.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.05 (6H, d, *J* = 6.4 Hz), 1.09 (6H, d, *J* = 6.8 Hz), 2.09–2.21 (2H, m), 2.60–2.69 (2H, m), 2.93–3.01 (2H, m), 3.28–3.36 (2H, m), 6.74–6.80 (2H, m), 7.02–7.06 (2H, m), 7.18–7.40 (8H, m); ^{31}P NMR ($CDCl_3$): δ 0.20; HRMS: calcd for $C_{28}H_{32}P_2$: 430.1978, found: 430.1960.

(+)-1-(2-diphenylphosphinophenyl)-2-isopropyl-2,3-dihydro-1*H*-phosphindole (iPr-mBeePHOS-Ph: (+)-3b)

A solution of 2-(diphenylphosphino)phenylphosphine (1.0 g, 3.40 mmol) in THF (30 mL) was cooled to 0 °C and 1.6M *n*-butyllithium in hexane (2.1 mL, 3.40 mmol) was added dropwise. After stirring 1 h at 0 °C, a solution of (+)-**7** (885 mg, 3.40 mmol) in THF (10 mL) was added. The reaction mixture was stirred for 1 h at 0 °C and then for 1 h at room temperature. The mixture was cooled to 0 °C and 1.6 M *n*-butyllithium in hexane (3.2 mL, 5.10 mmol) was added and stirred overnight at room temperature. The reaction mixture was treated with water (1 mL) and evaporated *in vacuo*. The residue was treated with water and extracted 3 times with diethyl ether. The combined extract was washed with water and evaporated *in vacuo*. Purification by silica gel column chromatography gave (+)-**3b** (400 mg, 27% yield).

Mp: 41–42 °C; $[\alpha]_D^{24}$: +84.7 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 0.81 (3H, d, *J* = 6.6 Hz), 0.83 (3H, d, *J* = 6.6 Hz), 1.81 (1H, qdd, *J* = 6.6, 6.6, 8.8 Hz), 2.24 (1H, m), 2.85 (1H, ddd, *J* = 4.9, 4.9, 16.5 Hz), 3.24 (1H, ddd, *J* = 4.4, 8.2, 16.5 Hz), 6.80–6.85 (1H, m), 6.93–6.98 (1H, m), 7.10–7.40

(16H, m); ^{31}P NMR ($CDCl_3$): δ –12.9 (d, *J* = 147.5), –0.4 (d, *J* = 147.5); HRMS: calcd for $C_{29}H_{28}P_2$: 438.1666, found: 438.1597.

(+)-1-[2-{Bis-(3,5-di-*t*-butyl-4-methoxyphenyl)phosphino}phenyl-2-isopropyl-2,3-dihydro-1*H*-phosphindole ((+)-DTBM-iPr-BeePHOS: (+)-3c)

The same procedure was used with this complex as was used for **3b** except that 2-{Bis-(3,5-di-*t*-butyl-4-methoxyphenyl)phosphino}phenylphosphine (1.00 g, 1,72 mmol) was added instead of 2-(diphenylphosphino)phenylphosphine, giving (+)-**3c** (337 mg, 27%).

Mp: 69–70 °C; $[\alpha]_D^{24}$: +8.45 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 0.69 (3H, d, *J* = 6.6 Hz), 0.71 (3H, d, *J* = 6.6 Hz), 1.29–1.34 (36H, m), 1.63–1.73 (1H, m), 2.00–2.06 (1H, m), 2.78–2.86 (1H, m), 3.12–3.21 (1H, m), 3.67 (3H, s), 3.69 (3H, s), 6.75–6.80 (1H, m), 6.87–6.92 (1H, m), 7.02–7.30 (9H, m), 7.31-–7.35 (1H, m); ^{31}P NMR ($CDCl_3$): δ –13.9 (d, *J* = 145.4 Hz), –1.4 (d, *J* = 145.4 Hz); HRMS: calcd for $C_{47}H_{64}O_2P_2$: 722.4382, found: 722.4397.

2-(2-Fluorophenyl)ethanol

To a suspension of lithium aluminium hydride (2.46 g, 64.0 mmol) in THF (50 mL) a solution of 2-furuorophenylacetic acid (10 g, 64.9 mmol) was added slowly at room temperature. After stirring for 1 h, Na_2SO_4•$10H_2O$ was slowly added followed by addition of Na_2SO_4. Filtration of the reaction mixture and evaporation *in vacuo* gave the product (8.83 g, 97% yield).

^{1}H NMR ($CDCl_3$): δ 1.48 (1H, bs), 2.93 (2H, t, *J* = 6.6 Hz), 3.87 (2H, td, *J* = 6.6, 6.6 Hz), 6.95–7.40 (4H, m); EI-MS: *m/z* 140 $(M)^+$

2-(2-Fluorophenyl)ethyl diisopropylcarbamate

A mixture of 2-(2-fluorophenyl)ethanol (8.0 g, 57.1 mmol), diisoopropylcarbamoyl chloride (9.34 g, 57.1 mmol) and pyridine (6.93 mL, 85.7 mmol) was heated to 90 °C and stirred overnight. After cooling to room temperature, The mixture was treated with 1 N HCl, extracted 3 times with ethyl acetate, washed with water, sat. $NaHCO_3$, water and brine and then dried over Na_2SO_4. After evaporation *in vacuo*, purification of the residue by silica gel chromatography gave the product (14.0 g, 98% yield).

^{1}H NMR ($CDCl_3$): δ 1.14 (12H, d, *J* = 6.8 Hz), 3.01 (2H, t, *J* = 6.8 Hz), 3.50–4.20 (2H, m), 4.31 (2H, t, *J* = 6.8 Hz), 6.95–7.30 (4H, m); EI-MS: *m/z* 267 $(M)^+$

2-(2-Fluorophenyl)-1-methylethyl diisopropylcarbamate

(–)-Sparteine (14.1 g, 60.2 mmol) in diethyl ether (75 mL) was cooled to –78 °C and 1.0M *s*-butyllithium in cyclohexane (60.2 mL, 60.2 mmol) was added dropwise. The reaction mixture was stirred for 15 min and then added to a solution of 2-(2-fluorophenyl)ethyl diisopropylcarbamate (10 g, 40.1 mmol) in diethyl ether at –78 °C. After stirring for 4 h, methyl iodide was added, followed by stirring for 2 h. Water was added and the resulting mixture was warmed to room temperature. The mixture was treated with 1 N HCl, extracted 3 times with ethyl acetate, washed with water and brine and then dried over Na_2SO_4. After evaporation *in vacuo*, purification of the residue by silica gel column chromatography gave the product (5.11 g, 45% yield).

^{1}H NMR ($CDCl_3$): δ 1.16 (12H, d, *J* = 6.8 Hz), 1.25 (3H, d, *J* = 6.4 Hz), 2.80–3.10 (2H, m), 3.60–4.15 (2H, m), 5.12 (1H, tq, *J* = 6.4, 6.8 Hz), 6.90–7.30 (4H, m).

(+)-1-(2-Fluorophenyl)propan-2-ol

To a solution of 2-(2-fluorophenyl)-1-methylethyl diisopropylcarbamate (5.11 g, 18.2 mmol) in THF, 1.0M diisobutylaluminium hydride in THF (182 mL, 182 mmol) was added dropwise. The reaction mixture was stirred overnight at room temperature and Na_2SO_4•$10H_2O$ was then slowly added. After addition of Na_2SO_4, the mixture was filtrated, evaporated *in vacuo* and purified by silica gel column chromatography, giving the product (2.15 g, 77% yield, 97% ee).

Optical purity was determined by GC (Chirasil DEX-CB).

$[\alpha]_D^{24}$: +27.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.25 (3H, d, *J* = 6.2 Hz), 1.50 (1H, d, *J* = 4.4 Hz), 2.74 (1H, ddd, *J* = 1.0, 7.4. 13.4 Hz), 2.86 (1H, ddd, *J* = 1.2, 5.2, 13.4 Hz), 3.95–4.20 (1H, m), 6.95–7.35 (4H, m); EI-MS: *m/z* 154 $(M)^+$

(+)-2-(2-Fluorophenyl)-1-methylethyl methanesulfonate

To a mixture of (+)-1-(2-fluorophenyl)-propan-2-ol (2.15 g, 14.0 mmol) and triethylamine (2.34 mL, 16.8 mmol) in dichloromethane (10 mL), methanesulfonyl chloride (1.19 mL, 15.4 mmol) was added at 0 °C. The resulting mixture was stirred overnight at room temperature and then treated with water and extracted 3 times with dichloromethane. The combined organic layer was then washed with water, evaporated *in vacuo* and purified by silica gel chromatography, giving the product (2.68 g, 82%).

$[\alpha]_D^{24}$: +23.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.48 (3H, d, *J* = 6.6 Hz), 2.62 (3H, s), 2.90–3.10 (2H, m), 4.95 (1H, qt, *J* = 6.6, 6.6 Hz), 6.95–7.40 (4H, m).

(+)-1,2-Bis(2-methyl-2,3-dihydroxy-1*H*-phosphindol-1-yl)benzene ((+)-BeePHOS: (+)-2a)

Except that (+)-2-(2-fluorophenyl)-1-methylethyl methanesulfonate (1.80 g, 7.74 mmol) was used instead of (+)-**7,** the same procedure that was used with **2b** was utilized with **2a** (367 mg, 25%).

Mp: 148–150 °C; $[\alpha]_D^{24}$: +301.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.42 (6H, dd, *J* = 7.7, 19.8 Hz), 2.74–2.81 (2H, m), 2.93 (2H, ddq, *J* = 2.7, 7.7, 7.7 Hz), 3.33–3.40 (2H, m), 6.53–6.60 (2H, m), 6.95–7.05 (2H, m), 7.26–7.32 (2H, m), 7.37–7.45 (2H, m), 7.56–7.60 (2H, m); ^{31}P NMR ($CDCl_3$): δ 10.3; Mill-MS: *m/z* 374.1321 (calc. 374.2353 for $C_{24}H_{24}P_2$).

(+)-1-(2-Diphenylphosphinophenyl)-2-methyl-2,3-dihydro-1*H*-phosphindole ((+)-mBeePHOS-Ph: (+)-3a)

The same procedure as **3b** was used except that (+)-2-(2-fluorophenyl)-1-methylethyl methanesulfonate (738 mg, 3.18 mmol) was used instead of (+)-**7**, giving **3a** (686 mg, 53%).

Mp: 40–42 °C; $[\alpha]_D^{24}$: +55.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.06 (3H, dd, *J* = 7.1, 20.0 Hz), 2.10–2.30 (1H, m), 2.63 (1H, ddd, *J* = 3.0, 6.8, 16.2 Hz), 3.31 (1H, ddd, *J* = 2.4, 7.6, 16.2 Hz), 6.65–6.70 (1H, m), 6.98–7.03 (1H, m), 7.07–7.12 (1H, m), 7.15–7.19 (1H, m), 7.28–7.40 (13H, m), 7.49–7.53 (1H, m); ^{31}P NMR ($CDCl_3$): δ –13.6 (d, *J* = 147.8 Hz), 7.7 (d, *J* = 147.8 Hz); EI-MS: *m/z* 410 $(M)^+$.

[Rh(cod)((+)-ipr-beephos)]OTf

A solution (+)-**2b** (50.0 mg, 0.116 mmol) in dichloromethane (2.5 mL) was added dropwise to a solution of $[Rh(cod)_2]OTf$ (54.3 mg, 0.116 mmol) in dichloromethane (5 mL). After stirring overnight at room temperature, the solvent was removed *in vacuo*. The residue was dissolved with dichloromethane (0.5 mL) and diethyl ether (5 mL) was slowly added, yielding an orange precipitate. The solution was then removed and the solid was washed twice with diethyl ether and dried *in vacuo* to afford the product (73.8 mg, 81%).

^{1}H NMR (CD_2Cl_2): δ 1.18 (6H, d, *J* = 6.6 Hz), 1.22 (6H, d, *J* = 6.6 Hz), 2.17–2.36 (8H, m), 2.47–2.55 (2H, m), 2.88–2.99 (2H, m), 3.11–3.17 (2H, m), 3.68–3.78 (2H, m), 5.03–5.10 (2H, m), 5.14–5.20 (2H, m), 7.11–7.15 (2H, m), 7.32–7.41 (4H, m), 7.47–7.54 (4H, m), 7.58–7.63 (2H, m); ^{31}P NMR (CD_2Cl_2): δ 73.4 (d, *J* = 151.5 Hz)

[Rh(cod)((+)- ipr-mbeephos-ph)]OTf

This complex was prepared in a manner analogous to that described above with the exception that (+)-iPr-mBeePHOS-Ph ((+)-**3b**) was used.

^{1}H NMR (CD_2Cl_2): δ 0.75 (3H, d, *J* = 6.6 Hz), 1.05 (3H, d, *J* = 6.6 Hz), 1.93–2.12 (3H, m), 2.17–2.34 (4H, m), 2.36–2.46 (2H, m), 2.86–2.95 (1H, m), 2.99–3.05 (1H, m), 3.59 (1H, ddd, *J* = 8.23, 16.5, 22.5 Hz), 4.83–4.93 (2H, m), 5.09–5.15 (1H, m), 5.21–5.28 (1H, m), 7.06–7.11 (1H, m), 7.28–7.36 (2H, m), 7.40–7.56 (12H, m), 7.56–7.65 (3H, m); ^{31}P NMR (CD_2Cl_2): δ 60.8 (dd, *J* = 25.6, 151.5 Hz), 72.2 (dd, *J* = 25.6, 145.1 Hz).

[Rh(cod)((+)-ipr-mbeephos-dtbm)]OTf

This complex was prepared in a manner analogous to that described above with the exception that (+)-iPr-mBeePHOS-DTBM ((+)-**3c**) was used.

^{1}H NMR (CD_2Cl_2): δ 0.85 (3H, d, *J* = 6.6 Hz), 1.11 (3H, d, *J* = 6.6 Hz), 1.36 (18H, s), 1.37 (18H, s), 2.03–2.20 (3H, m), 2.25–2.39 (4H, m), 2.43–2.50 (2H, m), 2.95–3.11 (2H, m), 3.65 (1H, ddd, *J* = 7.1, 15.9, 22.5 Hz), 4.87–4.94 (1H, m), 4.94–5.00 (1H, m), 5.11–5.18 (1H, m), 5.33–5.40 (1H, m), 7.10–7.14 (1H, m), 7.28–7.36 (3H, m), 7.40–7.46 (1H, m), 7.46–7.53 (4H, m), 7.55–7.64 (3H, m); ^{31}P NMR (CD_2Cl_2): δ 62.0 (dd, *J* = 25.6, 149.4 Hz), 70.5 (dd, *J* = 25.6, 147.3 Hz).

[Rh(cod)((+)-beephos)]OTf

This complex was prepared in a manner analogous to that described above with the exception that (+)-BeePHOS ((+)-**2a**) was used.

^{1}H NMR (CD_2Cl_2): δ 1.52–1.60 (6H, m), 2.17–2.38 (6H, m), 2.48–2.57 (2H, m), 3.05–3.20 (4H, m), 3.65–3.75 (2H, m), 5.08–5.16 (2H, m), 5.16–5.23 (2H, m), 7.23–7.30 (2H, m), 7.36–7.44 (4H, m), 7.48–7.52 (2H, m), 7.52–7.59 (2H, m), 7.60–7.65 (2H, m); ^{31}P NMR (CD_2Cl_2): δ 81.3 (d, *J* = 151.2 Hz).

[Rh(cod)((+)-mbeephos-ph)]OTf

This complex was prepared in a manner analogous to that described above with the exception that (+)-mBeephos-Ph ((+)-**3a**) was used.

^{1}H NMR (CD_2Cl_2): δ 1.30 (3H, dd, *J* = 7.1, 19.8 Hz), 2.04–2.60 (8H, m), 2.84–2.95 (1H, m), 2.98–3.03 (1H, m), 3.61 (1H, ddd, *J* = 8.2, 17.0, 18.7 Hz), 4.71–4.78 (1H, m), 4.90–4.98 (1H, m), 5.29–5.41 (2H, m), 7.22–7.27 (2H, m), 7.37–7.41 (2H, m), 7.43–7.75 (14H, m); ^{31}P NMR (CD_2Cl_2): δ 60.5 (dd, *J* = 27.7, 151.5 Hz), 78.2 (dd, *J* = 27.7, 149.4 Hz).

[RuCl(*p*-cymene)((+)-ipr-beephos)]Cl

(+)-iPr-BeePHOS ((+)-**2b**) (100 mg, 0.232 mmol) and [$RuCl_2$(*p*-cymene)]$_2$ (71.0 mg, 0.116 mmol) was dissolved in dichloromethane (2.5 mL) and ethanol (2.5 mL). The mixture was stirred

overnight at 50 °C and solvent was removed *in vacuo*. The remaining solid was washed 3 times with diethyl ether and dried *in vacuo*, affording the complex (165 mg, 97%).

^{1}H NMR (CD_2Cl_2): δ 0.50 (3H, d, *J* = 6.6 Hz), 0.53 (3H, d, *J* = 6.6 Hz), 1.01 (3H, d, *J* = 6.6 Hz), 1.02 (3H, d, *J* = 6.6 Hz), 1.14 (3H, d, *J* = 7.1 Hz), 1.23 (3H, d, *J* = 7.1 Hz), 1.62 (3H, s), 2.06–2.17 (1H, m), 2.37 (1H, qq, *J* = 7.1, 7.1 Hz), 2.64–2.80 (2H, m), 3.00–3.08 (1H, m), 3.47–3.67 (3H, m), 3.76 (1H, ddd, *J* = 8.2, 10.4, 17.0 Hz), 5.90–5.95 (1H, m), 6.07–6.11 (1H, m), 6.12–6.17 (1H, m), 6.31–6.36 (1H, m), 7.10–7.16 (1H, m), 7.24–7.34 (2H, m), 7.34–7.40 (1H, m), 7.42–7.50 (2H, m), 7.52–7.60 (4H, m), 7.60–7.65 (1H, m), 7.76–7.81 (1H, m); ^{31}P NMR (CD_2Cl_2): δ 87.1 (d, *J* = 36.3 Hz), 92.3 (d, *J* = 36.3 Hz).

[RuCl(*p*-cymene)((+)-ipr-mbeephos-ph)]Cl

This complex was prepared in a manner analogous to that described above with the exception that (+)-iPr-mBeePHOS-Ph ((+)-**3b**) was used.

^{31}P NMR (CD_2Cl_2): major δ 68.6 (d, *J* = 36.3 Hz), 82.3 (d, *J* = 36.3 Hz), minor δ 68.6 (d, *J* = 36.3 Hz), 84.3 (d, *J* = 36.3 Hz).

[RuCl(*p*-cymene)((+)-beephos)]Cl

This complex was prepared in a manner analogous to that described above with the exception that (+)-BeePHOS ((+)-**2a**) was used.

^{1}H NMR (CD_2Cl_2): δ 0.76 (3H, d, *J* = 7.1 Hz), 0.89 (3H, d, *J* = 7.1 Hz), 1.49 (3H, dd, *J* = 7.1, 18.7 Hz), 1.50 (3H, s), 1.64 (3H, dd, *J* = 7.1, 19.8 Hz), 2.21 (1H, qq, *J* = 7.1, 7.1 Hz), 3.07–3.19 (1H, m), 3.19–3.27 (1H, m), 3.33 (1H, ddd, *J* = 3.8, 10.4, 17.6 Hz), 3.56–3.70 (2H, m), 4.05 (1H, ddd, *J* = 7.7, 7.7, 17.6 Hz), 5.75–5.81 (1H, m), 5.94–6.00 (1H, m), 6.31–6.37 (1H, m), 6.49–6.57 (1H, m), 7.21–7.31 (2H, m), 7.32–7.41 (2H, m), 7.42–7.53 (3H, m), 7.53–7.61 (4H, m), 7.78–7.85 (1H, m); ^{31}P NMR (CD_2Cl_2): δ 86.3 (d, *J* = 36.3 Hz), 95.1 (d, *J* = 36.3 Hz).

[RuCl(*p*-cymene)((+)-mbeephos-ph)]Cl

This complex was prepared in a manner analogous to that described above with the exception that (+)-mBeePHOS-Ph ((+)-**3a**) was used.

^{31}P NMR (CD_2Cl_2): major δ 67.7 (d), 88.8 (d), minor δ 66.9 (d), 81.9 (d).

Ru(OAc)2((+)-ipr-beephos)

[RuCl(*p*-cymene)((+)-ipr-beephos)]Cl (100 mg, 0.136 mmol) and sodium acetate (27.9 mg, 0.34 mmol) were dissolved in dioxane (5 mL). The mixture was stirred overnight at 100 °C and then

cooled to room temperature followed by filtration. Evaporation *in vacuo* gave the complex. (63.6 mg, 72% yield)

^{1}H NMR (CD_2Cl_2): δ 0.51 (6H, d, *J* = 6.6 Hz), 1.07 (6H, d, *J* = 7.1 Hz), 1.10 (6H, s), 2.08–2.19 (2H, m), 2.93–3.02 (2H, m), 3.34–3.39 (2H, m), 3.43–3.52 (2H, m), 6.75–6.78 (2H, m), 7.07–7.10 (2H, m), 7.35–7.40 (4H, m), 7.47–7.50 (2H, m), 7.67–7.72 (2H, m); ^{31}P NMR (CD_2Cl_2): δ 111.7.

Ru(OAc)2((+)-ipr-mbeephos-ph)

This complex was prepared in a manner analogous to that described above with the exception that [RuCl(*p*-cymene)((+)-ipr-mbeephos-ph)]Cl was used.

^{1}H NMR (CD_2Cl_2): δ 0.34 (3H, d, *J* = 6.0 Hz), 1.03 (3H, *J* = 6.6 Hz), 2.96–3.05 (1H, m), 3.28–3.34 (1H, m), 3.41–3.52 (1H, m), 6.48–6.51 (1H, m), 6.99–7.05 (1H, m), 7.22–7.52 (12H, m), 7.58–7.68 (2H, m), 7.68–7.74 (1H, m), 7.74–7.80 (1H, m); ^{31}P NMR (CD_2Cl_2): δ 92.4 (d, *J* = 32.3 Hz), 111.2 (m).

General procedure for hydrogenation

A solid Rh or Ru complex catalyst was placed in a 100 mL stainless steel autoclave equipped with a Teflon-coated magnetic stirring bar, a pressure gauge and a gas inlet tube attached to a hydrogen source. Air present in the autoclave was replaced by nitrogen. Methanol and the substrate were added to the autoclave under a nitrogen stream. Air present in the gas inlet tube was removed by flushing with a stream of hydrogen. Hydrogen was initially introduced into the autoclave at a pressure of 0.4 MPa, before being reduced to 0.1 MPa by carefully releasing the stop valve. After this procedure was repeated three times, hydrogenation was carried out under the conditions listed in Table 1. The enantiomeric excesses and conversions were measured by GC or HPLC directly. The absolute configurations were determined by comparing elusion orders with the reported values.

Methyl *N*-acetylphenylalanine: Conversion and ee were determined by HPLC (Daicel Chiralcel OJ, hexane : 2-propanol = 90 : 10 (1.0 ml/min), 254 nm)

Methyl 3-hydroxyisobutyrate: Conversion and ee were determined by GLC (Cp Chirasil Dex-CB, 100 °C, He 151 kPa)