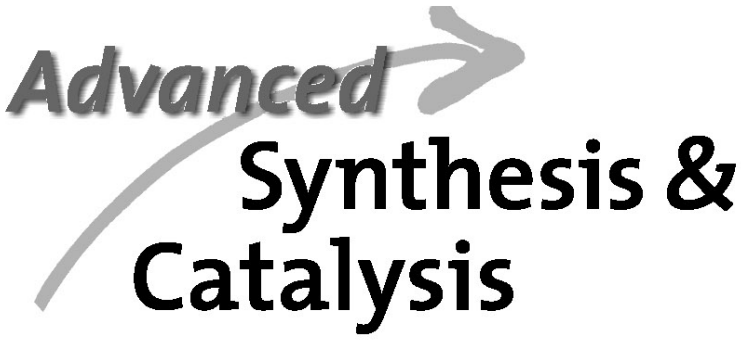

Supporting Information

A Convenient Synthesis of 2,2',6,6'-Tetramethoxy-4,4'-bis(dicyclo-hexylphosphino)-3,3'-bipyridine (Cy-P-Phos): Application in Rh-Catalyzed Asymmetric Hydrogenation of *a*-(Acylamino)acrylates

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Supporting Information

Optically pure (*S*)-**8a** was synthesized according to our previously reported procedures[6].

3-Bromo-2,6-dimethoxypyridine (5)

To a mechanically stirred mixture of 2,6-dimethoxypyridine (31.7 mL, 240 mmol) and carbon tetrachloride (400 mL), a solution of bromine (10.3 mL, 200 mmol) in carbon tetrachloride (50 mL) was slowly added at −30 °C to −40 °C over 12 h. The solution was neutralized to pH = 7.5 with sodium carbonate at 0 °C followed by thrice extraction with dichloromethane (100 ml each). The combined extracts were dried with anhydrous Na_2SO_4 and the solvent was removed with a rotovapor to give the crude product which was purified by distillation under vacuo to furnish 30.3 g (70% of theoretical yield) of pure product as a colorless oil (67−74 °C/0.05mmHg). ^{1}H NMR ($CDCl_3$, 500 MHz): *d* 3.89 (s, 3H), 3.99 (s, 3H), 6.22 (d, *J* = 8.5 Hz, 1H), 7.62 (d, *J* = 8.5 Hz, 1H).

3-Bromo-2,6-dimethoxy-4-diphenylphosphinopyridine (6a)

To a magnetically stirred solution of 35 mL (70 mmol) of ca. 2.0 M LDA (lithium diisopropylamide) a solution of 3-bromo-2,6-dimethoxypyridine (**5**, 11.7 g, 53.5 mmol) in dried THF (80 mL) was added at −78 °C over 20 minutes by syringe. To the resulting red-brown suspension, a solution of diphenylphosphine chloride (59 mmol) in 80 mL THF was added at −78 °C under a N_2 atmosphere. The reaction mixture was allowed to warm up by itself to room temperature and stirred at room temperature overnight. The reaction was worked up with 10 mL

water and the solvent was removed with a rotovapor. The organic product was extracted with CH_2Cl_2 (3 × 50 mL). The combined extract was washed with water (2 × 50 mL) and was dried with anhydrous sodium sulfate and concentrated in vacuo to give the crude product which was recrystallized in methanol to provide a white powder product (90 % yield). ^{1}H NMR ($CDCl_3$, 500 MHz): *d* 3.83 (s, 3H), 4.01 (s, 3H), 5.71 (d, *J* = 3.0 Hz, 1H), 7.28–7.38 (m, 10H). ^{31}P NMR ($CDCl_3$, 202 MHz): *d* –4.26.

3-Bromo-2,6-dimethoxy-4-diphenylphosphinoylpyridine (7a)

To a magnetically stirred solution of 3-bromo-2,6-dimethoxy-4-diphenylphosphinopyridine (**6a**, 6.0 g, 15.0 mmol) in 150 mL acetone, 10 mL of ca. 35% hydrogen peroxide was added slowly at 0 °C. The reaction was monitored by thin-layer chromatography and the product was extracted with CH_2Cl_2 (3 × 100 mL). The combined extract was washed with water (3 × 20 mL) and dried with anhydrous sodium sulfate. The filtrate was concentrated in vacuo to give a white powder (6.2 g, 99% yield). ^{1}H NMR ($CDCl_3$, 500 MHz): *d* 3.89 (s, 3H), 4.00 (s, 3H), 6.30 (d, *J* = 13.0 Hz, 1H), 7.46–7.50 (m, 4H), 7.56–7.58 (m, 2H), 7.69–7.73 (m, 4H). ^{31}P NMR ($CDCl_3$, 202 MHz): *d* 30.78.

2,2',6,6'-Tetramethoxy-bis(diphenylphosphinoyl)-3,3'-bipyridine ((±)-8a)

A mixture of 3-bromo-2,6-dimethoxy-4-di(4-methylphenyl)phosphinoylpyri-dine (**7a**, 4.85 g, 11.6 mmol), Cu powder (3 g, 46.4 mmol) and dried DMF (12.5 mL) was stirred at 140 °C for 13 h. The mixture was evaporated to dryness, then $CHCl_3$ (50 mL) was added and the mixture was refluxed for a few minutes. Insoluble solid was removed by filtration and was washed with $CHCl_3$ (150 mL). The combined filtrate was dried with anhydrous sodium sulfate and the solvent was evaporated. The solid residue was washed with ethyl acetate (20 mL) to give a white pure powdery product (3.14 g, 80% yield). ^{1}H NMR ($CDCl_3$, 500 MHz): *d* 3.33 (s, 6H), 3.83 (s, 6H), 6.13 (d, *J* = 13.8 Hz, 2H), 7.33–7.35 (m, 4H), 7.41–7.45 (m, 6H), 7.50–7.59 (m, 6H), 7.64–7.69 (m, 4H). ^{31}P NMR ($CDCl_3$, 202 MHz): *d* 30.91.

Optical Resolution of (±)-8a with (–) or (+)-2,3-*O,O'*-Dibenzoyltartaric Acid Monohydrate

To a refluxing solution of 2.40 g (3.55 mmol) of racemic 2,2',6,6'-tetramethoxy-bis(diphenylphosphinoyl)-3,3'-bipyridine ((±)-**8a**) in 39 mL $CHCl_3$, a solution of 1.33 g (3.55 mmol) of (+)-2,3-*O,O'*-dibenzoyltartaric acid monohydrate[*D*-(+)-DBT] in 39 mL ethyl acetate was added slowly. The mixture was stirred under reflux for 30 min and then allowed to stand at room temperature overnight. The crystals formed are collected on a glass funnel and the filtrate is stored for recovery of the other enantiomer. The white solid product was dried in vacuo at room

temperature (0.1 mm Hg) for 2 h to give a 1 : 1 complex (*S*)-**8a**-(+)-DBT [1.69 g, 92% yield based on (±)-**8a** initially used] as needles, which was treated with 10% aq. NaOH (25 mL) and the mixture was extracted with three 20 mL portions of chloroform. The combined organic layer was washed with 10% aq. NaOH (20 mL), water (2 × 10 mL) and dried over anhydrous sodium sulfate. Evaporation of the solvent furnished white solid (*S*)-**8a** [1.02g, 85% yield based on (±)-**8a** initially used].

Optical purities of the resolved **8a** were determined by HPLC analysis (Diacel-AD column, eluted by hexane:2-propanol = 20 : 80, flow rate = 1.0 mL/min, ?detection = 254 nm, t_R of (*S*)-**8a**, 13 min; t_R of *R* isomer, 20 min). Thus, enantiomeric excess of (*S*)-**8a** was found to be over 99.0%.

(*S*)-2,2',6,6'-Tetramethoxy-4,4'-bis(dicyclohexylphosphinoyl)-3,3'-bipyridine [(*S*)-9]

Optically pure (*S*)-2,2',6,6'-tetramethoxy-bis(diphenylphosphinoyl)-3,3'-bipyridine [(*S*)-**8a**, 500 mg, 0.739 mmol], PtO_2 (75 mg, 0.33 mmol) and 15 mL glacial acetic acid were charged into a 50 mL autoclave equipped with a magnetic stirring bar. The autoclave was then charged with 500 psi of H_2. The mixture was stirred for 5 days at 50 °C. After releasing the hydrogen gas and filtering off the solid catalyst, the solution was evaporated to dryness. The residue was dissolved in 10 mL acetone and neutralized with aqueous NaOH solution followed by extraction with three portions of 20 mL chloroform. The combined extract was washed with water for three times and dried with anhydrous sodium sulfate. The solvent was removed to give the product as a white solid (462.5 mg, 93% yield). M.p. 326 ℃ (decompose), $[\alpha]_D^{20}$ = -70.4° (c = 1.01, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 500 MHz): *d* 1.08–1.99 (m, 42H), 2.07–2.16 (m, 2H), 3.79 (s, 6H), 3.93 (s, 6H), 6.22 (d, *J* = 10.5 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125.7 MHz): *d* 25.05, 26.08, 26.18, 26.22, 26.30, 26.34, 26.77, 26.87, 26.95, 27.05, 27.14, 27.23, 29.47, 31.96, 36.90, 37.42, 38.01, 38.52, 53.55,101.38, 101.48, 114.89, 114.91, 114.95, 144.01, 144.65, 161.20, 161.28, 161.38. ^{31}P NMR ($CDCl_3$, 202 MHz): *d* 46.25. LSMS: 701 [M^+], 702 [M^+ + 1]. Anal. calcd. for $C_{38}H_{58}N_2O_6P_2$: C, 65.12; H, 8.34; N, 4.00. Found: C, 65.65; H, 8.28; N, 4.06.

(*S*)-2,2',6,6'-Tetramethoxy-bis(dicyclohexylphosphino)-3,3'-bipyridine [(*S*)-Cy-P-Phos, (*S*)-4d]

(*S*)-**6** (1.75 g, 2.5 mmol), dry, degassed toluene (50 mL), triethylamine (3.9 mL, 28.6 mmol) and trichlorosilane (3.5 mL, 28.6 mmol) were charged into a three-necked flask, fitted with a thermometer and a reflux condenser,. The mixture was stirred and heated at 100 °C for 1 h and finally at reflux for 48 h. After the solution was cooled to room temperature, 40 mL of 20%

aqueous sodium hydroxide solution was carefully added. The mixture was then stirred at 80 °C until the organic and aqueous layers were clear. The aqueous layer was separated and extracted with two 50-mL portions of warm toluene. The combined organic layer was washed with 20 mL of 20% sodium hydroxide solution and two 40 mL portions of brine and then dried over anhydrous sodium sulfate. The organic layer was concentrated under reduced pressure and the residual was purified by short-column flash chromatography under nitrogen using dichloromethane as an eluent to give the title phosphine as a white solide (886 mg, 53% yield). M.p. 258 ℃ (decompose), $[a]_D^{20}$ = -87.4 (*c* 0.50, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 500 MHz): *d* 1.09–1.28 (m, 20H), 1.51–1.78 (m, 22H), 1.93 (s, 2H), 3.80 (s, 6H), 3.96 (s, 6H), 6.46 (s, 2H). ^{13}C NMR ($CDCl_3$, 125.7 MHz): *d* 25.42, 25.70, 26.06, 26.10, 26.14, 26.19, 26.77, 26.81, 26.84, 26.88, 26.92, 27.89, 27.92, 27.97, 28.84, 28.91, 28.98, 29.43, 29.48, 29.54, 29.92, 30.00, 30.07, 31.55, 31.62, 31.67, 34.25, 34.31, 34.37, 52.07, 52.25, 115.64, 115.78, 115.91, 151.73, 159.49, 159.53, 159.57, 160.24. ^{31}P NMR ($CDCl_3$, 202 MHz): *d* –9.82. LSMS: 669 [M^+], 670 [M^+ + 1]. Anal. calcd. for $C_{38}H_{58}N_2O_4P_2$: C, 68.24; H, 8.74; N, 4.19. Found: C, 67.97; H, 8.90; N, 4.10.