Supporting Information

© Wiley-VCH 2006

69451 Weinheim, Germany
Synthesis of Triphosphorous Bidentate Phosphine-Phosphoramidite Ligands and their Application in Highly Enantioselective Hydrogenation of ortho-Substituted Aryl Enamides

Weicheng Zhang and Xumu Zhang

Department of Chemistry, the Pennsylvania State University, University Park, PA 16802

All operations were carried out using standard Schlenk techniques unless mentioned otherwise. The degassed dry solvents are used for all experiments. Diphenylchlorophosphine, (1S, 1′S, 2R, 2′R)-Tangphos, and (R,R)-Et-DuPhos were purchased from Strem Inc., and all other chemicals were purchased from Aldrich or Acros Inc. The substrates were prepared according to literature.1 NMR data were recorded on Bruker DPX-300, CDPX-300, and Avance-360 spectrometers. MS data were recorded on KRATOS mass spectrometer for LR-APCI and HR-APCI. Optical rotation was recorded on a Perkin-Elmer 241 polarimeter. MM2 calculations were carried out with CAChe® program (CAChe Worksystem Pro version 6.1, Fujitsu Ltd.). Thin layer chromatography (TLC) was performed on EM reagents 0.25 mm silica 60-F plates. Column chromatography was performed using 200-400 mesh silica gel from Natland International Inc. Chiral GC analysis was carried out on Helwett-Parkard 6890 gas chromatography equipped with chiral capillary column (carrier gas: He at 1 mL/min). Chiral HPLC analysis was carried out on a Waters 600 chromatography at 25°C.

1. Synthesis and characterization of 1 (page S1-S4)
(a) (R)-2,2′-bis(methoxymethoxy)-1,1′-binaphthyl ((R)-BINOL-MOM)
The synthesis of (R)-BINOL-MOM followed literature procedure.\(^2\)

(b) (R)-2,2'-bis(methoxymethoxy)-3,3'-bis(diphenylphosphino)-1,1'-binaphthyl (2)

Toward a solution of BINOL-MOM (10 mmol, 3.744 g) in Et\(_2\)O (170 mL) charged into a flame-dried argon filled Schlenk flask was added \(n\)-BuLi (2.5M in hexane, 30 mmol, 12 mL) dropwise at room temperature, and stirred for 3 hours. THF (110 mL) was added and stirred for 1 hour. After the reaction mixture was cooled to 0°C, ClPPh\(_2\) (30 mmol, 5.56 mL) was quickly added. The solution was stirred for 1 hour, and quenched with saturated aqueous NH\(_4\)Cl. The solvent was removed and the residue was dissolved in EtOAc and washed with water, brine, and dried with Na\(_2\)SO\(_4\). After being concentrated, the product 2 was recrystallized from CH\(_2\)Cl\(_2\)/hexane as light yellow crystals. (5.18g, yield 70%) \(^1\)H NMR (300 MHz, CD\(_2\)Cl\(_2\)): \(\delta = 2.75\) (s, 6H), 4.68 (dd, 4H, \(J_1 = 18\) Hz, \(J_2 = 3\) Hz), 7.23-7.44 (m, 28H), 7.62-7.65 (d, 2H, \(J = 9\) Hz). \(^13\)C NMR (75 MHz, CD\(_2\)Cl\(_2\)): \(\delta = 56.85, 56.91, 99.13, 99.23, 125.47, 126.41, 127.23, 128.44, 128.94, 128.96, 129.94, 129.06, 129.34, 129.39, 131.20, 133.22, 134.38, 134.49, 134.65, 134.76, 134.76, 136.88, 155.58. \(^{31}\)P NMR (146 MHz, CD\(_2\)Cl\(_2\)): \(\delta = -14.69\) (s). HRMS (M+Na\(^+\)): calculated: 765.2300; found: 765.2279.

(c) (R)-3,3'-bis(diphenylphosphino)-1,1'-binaphthyl-2,2'-diol (3)

In a flame-dried argon filled Schlenk flask was charged 2 (400 mg, 0.539 mmol), MeOH (50 mL), and 10 drops of concentrated HCl (aqueous 35 wt%). The reaction mixture was stirred at 60°C for 1 hour. Then the solvent was removed, and the residue
was dissolved in EtOAc. Degassed saturated NaHCO3 solution and brine were used to washed the solution. Then it was dried with Na2SO4. After being concentrated, it was purified through a short column of silica gel (eluent CH2Cl2) to afford the product 3 as white powder. (278 mg, 79% yield) 1H NMR (300 MHz, CD2Cl2): δ = 5.49 (s, 2H), 7.11-7.13 (m, 2H), 7.29-7.32 (m, 4H), 7.40-7.46 (m, 22H), 7.63-7.67 (m, 2H). 13C NMR (75 MHz, CD2Cl2): δ = 111.68, 111.70, 124.17, 124.47, 128.05, 128.87, 128.93, 129.03, 129.12, 129.43, 129.52, 129.74, 129.76, 134.08, 134.18, 134.30, 134.35, 134.56, 134.87, 153.88. 31P NMR (146 MHz, CD2Cl2): δ = -17.43 (s). HRMS (M+H+): calculated: 655.1956; found: 655.1926.

(d) (R)-O,O′-(3,3′-bis(diphenylphosphino)-1,1′-dinaphthyl-2,2′-diyl)-N,N-dimethylphosphorous amidite (1a)

In a flame-dried argon filled Schlenk tube was charged 3 (563 mg, 0.86 mmol) and toluene (20 mL). Then hexamethylphosphorous triamide (HMPT, 0.2 mL, 1.12 mmol) was added. The reaction mixture was stirred at 110°C overnight. After being concentrated, the product was purified through a silica gel column (EtOAc/hexane = 1:15) to afford the product 1a as white powder. (550.4 mg, yield 88%) 1H NMR (300 MHz, CD2Cl2): δ = 2.54 (d, J = 9.3 Hz), 7.24-7.46 (m, 28H), 7.61-7.68 (m, 2H). 13C NMR (75 MHz, CD2Cl2): δ = 35.77, 35.86, 36.01, 36.14, 122.63, 128.68, 128.74, 128.82, 128.91, 128.98, 129.05, 129.08, 129.10, 129.20, 133.52, 133.78, 133.97, 134.23, 135.04, 135.32. 31P NMR (146 MHz, CD2Cl2): δ = -16.98 (d, J_p-p = 17.9 Hz), -12.62 (d, J_p-p = 4.5 Hz), 149.53 (d, J_p-p = 16.9 Hz). HRMS (M+H+): calculated: 728.2037; found: 728.2014.

(e) (R)-O,O′-(3,3′-bis(diphenylphosphino)-1,1′-dinaphthyl-2,2′-diyl)-N,N-diethylphosphorous amidite (1b)
In a flame-dried argon filled Schlenk tube was charged 3 (253 mg, 0.39 mmol) and toluene (10 mL). Then hexaethylphosphorous triamide (HEPT, 0.15 mL, 0.54 mmol) was added. The reaction mixture was stirred at 110°C overnight. After being concentrated, the product was purified through a silica gel column (EtOAc/hexane = 1:10) to afford the product 1b as white powder. (234 mg, yield 80%) \(^1\)H NMR (300 MHz, CD\(_2\)Cl\(_2\)): \(\delta = 0.92\) (t, \(J = 7.1\) Hz), 2.95 (m, 4H), 7.22-7.51 (m, 28H), 7.59-7.67 (m, 2H). \(^{13}\)C NMR (75 MHz, CD\(_2\)Cl\(_2\)): \(\delta = 15.39, 15.44, 15.49, 40.27, 40.32, 40.56, 40.61, 124.87, 128.64, 128.73, 128.77, 128.83, 128.87, 129.03, 129.06, 129.09, 129.13, 133.55, 133.82, 134.00, 134.28, 134.99, 135.27, 137.07. \(^{31}\)P NMR (146 MHz, CD\(_2\)Cl\(_2\)): \(\delta = -13.05\) (d, \(J_{P-P} = 30.3\) Hz), -11.43 (s), 150.57 (d, \(J_{P-P} = 30.1\) Hz). HRMS (M+H\(^+\)): calculated: 756.2350; found: 756.2328.
2. $^{31}$P-NMR spectrum of $[\text{Rh(COD)1a}]\text{BF}_4$ (page S5)
3. Characterization of new compounds 4l, 4m, 5l, and 5m (page S6-S7)

(1) N-(1-(2-nitrophenyl)ethyl)acetamide 4l

\[
\begin{align*}
\text{NHAc} &\quad \text{NO}_2 \\
\end{align*}
\]

$^1$H NMR (300 MHz, CD$_2$Cl$_2$): $\delta$ = 1.94 (s, 3H), 4.76 (s, 1H), 5.54 (s, 1H), 7.31 (s, 1H), 7.48-7.54 (m, 2H), 7.60-7.65 (m, 2H), 7.87-7.90 (m, 1H). $^{13}$C NMR (75 MHz, CD$_2$Cl$_2$): $\delta$ = 23.93, 104.68, 124.31, 129.72, 132.13, 133.41, 133.63, 139.26, 148.48, 168.89. HRMS (M+Na$^+$): calculated: 229.0589, found: 229.0571.

(2) N-(1-(2-trifluoromethylphenyl)ethyl)acetamide 4m

\[
\begin{align*}
\text{CF}_3 &\quad \text{NHAc} \\
\end{align*}
\]

$^1$H NMR (300 MHz, CD$_2$Cl$_2$): $\delta$ = 1.99 (s, 3H), 4.70 (s, 1H), 5.90 (s, 1H), 6.80 (s, 1H), 7.47-7.71 (m, 4H). $^{13}$C NMR (75 MHz, CD$_2$Cl$_2$): $\delta$ = 24.26, 103.88, 122.68, 126.31, 126.48, 126.55, 126.62, 126.69, 128.23, 128.63, 129.02, 131.98, 132.33, 137.81, 137.84, 139.49, 169.04. HRMS (M+Na$^+$): calculated: 252.0612, found: 252.0614.

(3) N-Acetyl-1-(2-nitrophenyl)ethylamine 5l

\[
\begin{align*}
\text{NHAc} &\quad \text{NO}_2 \\
\end{align*}
\]

$^1$H NMR (300 MHz, CD$_2$Cl$_2$): $\delta$ = 1.49 (d, $J$ = 7.0 Hz, 3H), 1.90 (s, 3H), 5.37-5.42 (m, 1H), 6.38 (s, br, 1H), 7.39-7.42 (m, 1H), 7.50-7.60 (m, 2H), 7.81-7.85 (m, 1H). $^{13}$C NMR (75 MHz, CD$_2$Cl$_2$): $\delta$ = 21.75, 23.09, 46.22, 124.78, 128.23, 128.29, 133.68, 139.63, 139.64, 169.61. $[\alpha]_D^{20}$ = -117.2° (GC 98.2% ee, $c$ 0.85, CHCl$_3$). HRMS (M+ Na$^+$): calculated: 231.0746, found: 231.0751.

(4) N-Acetyl-1-(2-trifluoromethylphenyl)ethylamine 5m

\[
\begin{align*}
\text{CF}_3 &\quad \text{NHAc} \\
\end{align*}
\]

$^1$H NMR (300 MHz, CD$_2$Cl$_2$): $\delta$ = 1.40 (d, $J$ = 6.9 Hz, 3H), 1.90 (s, 3H), 5.31-5.35 (m, 1H), 6.60 (s, br, 1H), 7.33-7.39 (m, 1H), 7.54-7.56 (m, 2H), 7.62-7.65 (m, 1H). $^{13}$C NMR
(75 MHz, CD$_2$Cl$_2$): $\delta = 23.22, 23.37, 46.12, 46.15, 46.18, 46.22, 126.11, 126.19, 126.27, 126.35, 126.72, 127.21, 127.44, 127.54, 132.81, 132.82, 144.19, 144.21, 169.50. [\alpha]_D^{20} = +71.7^\circ$ (GC 94.2% ee, c 0.71, CHCl$_3$). HRMS (M+Na$^+$): calculated: 254.0769, found: 254.0774.

4. Chiral GC and HPLC conditions for the determination of ee (page S7-S9)

(1) N-Acetyl-1-phenylethylamine (5a): GC, $\beta$-dex 390, 150°C, $t_S = 22.8$ min, $t_R = 23.8$ min

(2) N-Acetyl-1-(3-methylphenyl)ethylamine (5b): GC, $\beta$-dex 390, 140°C, $t_S = 51.3$ min, $t_R = 54.9$ min

(3) N-Acetyl-1-(4-trifluoromethylphenyl)ethylamine (5c): GC, $\beta$-dex 390, 150°C, $t_S = 30.8$ min, $t_R = 32.4$ min

(4) N-Acetyl-1-(4-trifluoromethylphenyl)propylamine (5d): GC, $\beta$-dex 390, 160°C, $t_S = 23.4$ min, $t_R = 24.7$ min

(5) N-Acetyl-1-(4-methoxyphenyl)propylamine (5e): HPLC, $(R,R)$-Poly Whelk-0 from Regis Technologies Inc., 1 mL/min, iPrOH/hexane = 90:10, $t_S = 12.37$ min, $t_R = 35.78$ min
(6) \(N\)-Acetyl-1-(2-naphthyl)ethylamine (5f): HPLC, \((R,R)\)-Poly Whelk-0 from Regis Technologies Inc., 1 mL/min, \(iPrOH/hexane = 70:30\), \(t_S = 5.78\) min, \(t_R = 50.03\) min

(7) \(N\)-Acetyl-1-(2-naphthyl)propylamine (5g): HPLC, \((R,R)\)-Poly Whelk-0 from Regis Technologies Inc., 1 mL/min, \(iPrOH/hexane = 80:20\), \(t_S = 6.82\) min, \(t_R = 59.90\) min

(8) \(N\)-Acetyl-1-(2-methylphenyl)ethylamine (5h): GC, \(\gamma\)-dex 225, 140°C, \(t_S = 54.6\) min, \(t_R = 58.7\) min

(9) \(N\)-Acetyl-1-(2-methoxyphenyl)ethylamine (5i): GC, \(\gamma\)-dex 225, 150°C, \(t_S = 45.2\) min, \(t_R = 47.1\) min

(10) \(N\)-Acetyl-1-(2-fluorophenyl)ethylamine (5j): GC, \(\gamma\)-dex 225, 150°C, \(t_S = 21.2\) min, \(t_R = 26.8\) min

(11) \(N\)-Acetyl-1-(2-chlorophenyl)ethylamine (5k): GC, \(\gamma\)-dex 225, 150°C, \(t_S = 53.8\) min, \(t_R = 62.5\) min

(12) \(N\)-Acetyl-1-(2-nitrophenyl)ethylamine (5l): GC, \(\gamma\)-dex 225, 170°C, \(t_{\text{minor}} = 48.8\) min, \(t_{\text{major}} = 51.6\) min
(13) $N$-Acetyl-1-(2-trifluromethylphenyl)ethylamine (5m): GC, $\gamma$-dex 225, 150°C, $t_{\text{minor}} = 22.5$ min, $t_{\text{major}} = 23.9$ min

(14) $N$-Acetyl-1-(1-naphthyl)ethylamine (5n): GC, $\gamma$-dex 225, 180°C, $t_S = 54.9$ min, $t_R = 60.0$ min