Supporting Information
for DOI: 10.1055/s-0028-1088198
© Georg Thieme Verlag KG Stuttgart · New York 2008
Rhodium-Catalyzed Asymmetric 1,4-Addition of Heteroaryl Cyclic Triolborate to α,β-Unsaturated Carbonyl Compounds

Xiao-Qiang Yu, Yasunori Yamamoto*, Norio Miyaura *

Division of Chemical Process Engineering, Graduate School of Engineering, Hokkaido University, Kita 13, Nishi 8, Sapporo 060-8628, Japan
yasuyama@eng.hokudai.ac.jp; miyaura@eng.hokudai.ac.jp

Supporting Information

General Information:
Infrared (IR) spectra were recorded on a Thermo Nicolet AVATAR 320 FT–IR. Wavelength of maximum absorbance is quoted in cm\(^{-1}\). \(^1\)H–NMR spectra were recorded on a JEOL JNM–400II (400 MHz) in CDCl\(_3\) (\(\delta_H = 7.25\)) with tetramethylsilane as an internal standard. Chemical shifts are reported in part per million (ppm), and signal are expressed as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (br). \(^{13}\)C–NMR spectra were recorded on a JEOL JNM–400II (100MHz) in CDCl\(_3\) (\(\delta_C = 77.0\)) with tetramethylsilane as an internal standard. Chemical shifts are reported in part per million (ppm). HPLC analysis was directly performed with chiral stationary phase column, Chiralcel OD–H, AD, AD–H, OJ–H, and OB–H purchased from Dicel Co., Ltd. High resolution mass (HR–MS) spectra were recorded on a JEOL JMS AX–500 or a JEOL JMS–SX102A mass spectrometers at the Center for Instrumental Analysis, Hokkaido University. Optical rotations were measured on a HORIBA SEPA–300 digital polarimeter. Kanto Chemical silica gel (60, particle size 0.063–0.210 mm) was used for flash column chromatography. \([\text{Rh(cod)}_2]BF_4\), \([\text{RhCl}(\text{coe})_2]_2\), \([\text{RhCl}($CH_2$)$_2$]_2\), and \([\text{Rh(nbd)}_2]BF_4\) were prepared by the literature procedure. \([\text{RhOH(cod)}]_2\) was commercial available from Aldrich. 1,4-dioxane was purchased from Wako.

Lithium Heteroarylborates (2): Lithium heteroaryl cyclic triolborates were prepared by the literature procedure.\(^5\) Lithium 2-pyridyl(triol)borate (2a): n-BuLi (110 mmol) in hexane was added to a stirred solution of 2-bromopyridine (100 mmol) in THF (400 mL) at -78 °C. The resulting mixture was stirred for 1h at -78 °C, then a solution of triisopropyl borate (120 mmol) was added. The mixture was stirred for 2 h at -78 °C and then allowed to warm to room temperature. A solution of 1,1,1-tris(hydroxymethyl)ethane (100 mmol) in THF (150 mL) was then added, and the resulting mixture was stirred for 5 h. Concentration to dryness under reduced pressure gave 2a (82%). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)) \(\delta = 0.54\) (s, 3H), 3.67 (s, 6H), 7.06–7.51(m, 3H), 8.24 ppm (br s, 2H); \(^{13}\)C NMR (100 MHz, DMSO-d\(_6\)): \(\delta = 15.9, 73.5, 120.8, 127.8, 134.4, 146.9\) ppm; \(^{11}\)B NMR (128 MHz, DMSO-d\(_6\)): \(\delta = 3.25\) ppm.

Typical procedure for rhodium-catalyzed asymmetric conjugate additions of
heteroaryl cyclic triolborates to α,β-unsaturated carbonyl compounds:

Heteroaryl cyclic triolborate (1.0 mmol), [Rh(nbd)\textsubscript{2}]BF\textsubscript{4} (0.025 mmol) and with (S)-binap (0.0275 mmol) or (R)-bipam (0.0275 mmol) was added to a 10 mL-flask containing a magnetic stirring bar, a septum inlet, and a reflux condenser. The flask was flushed with argon and charged with 1,4-dioxane (3.0 ml), then the mixture was stirred for 30 min at room temperature. After addition of an unsaturated carbonyl compound (0.5mmol), the mixture was stirred for 16–20h at 90 °C. The reaction was quenched with NH\textsubscript{4}Cl (sat.) for 0.5 h. The product was extracted with AcOEt, washed with brine, and dried over anhydrous MgSO\textsubscript{4}. Chromatography over silica gave the desired product.

The spectra of compounds 3j, 3k, and 3l are identical to those reported in the literature.\textsuperscript{6}

(S)-3-(6-Methoxy-3-pyridyl)-cyclohexanone (3a)
IR (neat) \(\nu = 2928, 1709, 1573, 1466, 1209, 798 \text{ cm}^{-1}\); \(^1\text{H} \text{NMR} (400 \text{ MHz, CDCl}_3) \delta = 1.77–1.84 (m, 2H), 2.05–2.07 (m, 1H), 2.14–2.18 (m, 1H), 2.37–2.59 (m, 4H), 2.95-2.98 (m, 1H); \(^13\text{C} \text{NMR} (100 \text{ MHz, CDCl}_3) \delta = 25.3, 32.6, 41.0, 41.4, 48.7, 53.3, 110.8, 132.2, 136.9, 144.7, 146.9, 163.1, 210.2; \ [\alpha]_{20}^D = -29.6 ^\circ (c \ 1.00, \text{CHCl}_3); \text{HPLC (AD–H, 7% i-PrOH in hexane, 0.5 mL/min, 230 nm): t} \text{major} = 27.6 \text{ min, t} \text{minor} = 26.1 \text{ min, 97% ee; HR–MS (EI): calcd for C}_{12}\text{H}_{15}\text{NO}_2 (M) 205.1103 found 205.1100.}

(S)-3-(6-Methoxy-3-pyridyl)-cyclopentanone (3b)
IR (neat) \(\nu = 2947, 1739, 1494, 1338, 1284, 830 \text{ cm}^{-1}\); \(^1\text{H} \text{NMR} (400 \text{ MHz, CDCl}_3) \delta = 1.94–1.98 (m, 1H), 2.23–2.46 (m, 4H), 2.65 (dd, \(J = 7.2, 18.0 \text{ Hz, 1H}), 3.36–3.39 \text{ (m, 1H)}, 3.93 (s, 3H), 6.74 (d, \(J = 8.8 \text{ Hz, 1H}), 7.48 (d, \(J = 8.8 \text{ Hz, 1H}), 8.06 (s, 1H); \(^13\text{C} \text{NMR} (100 \text{ MHz, CDCl}_3) \delta = 30.9, 38.6, 38.9, 45.4, 53.2, 110.7, 130.8, 136.8, 144.8, 163.1, 217.4; \ [\alpha]_{20}^D = -1.4 ^\circ (c \ 1.00 \text{ CHCl}_3); \text{HPLC (OD–H, 5% i-PrOH in hexane, 0.5 mL/min, 230 nm): t} \text{major} = 54.7 \text{ min, t} \text{minor} = 70.0 \text{ min, 92% ee; HR–MS (EI): calcd for C}_{11}\text{H}_{13}\text{NO}_2 (M) 191.0946 found 191.0950.}

(S)-3-(6-Methoxy-3-pyridyl)-cycloheptanone (3c)
IR (neat) \(\nu = 2928, 1697, 1492, 1287, 1026, 832 \text{ cm}^{-1}\); \(^1\text{H} \text{NMR} (400 \text{ MHz, CDCl}_3) \delta = 1.48–1.54 (m, 1H), 1.66–1.76 (m, 2H), 1.98–2.07 (m, 3H), 2.57–2.63 (m, 3H), 2.87–2.94 (m, 2H), 3.91 (s, 3H), 6.70 (d, \(J = 8.4 \text{ Hz, 1H}), 7.40 (d, \(J = 8.4 \text{ Hz, 1H}), 7.99 (s, 1H); \(^13\text{C} \text{NMR} (100 \text{ MHz, CDCl}_3) \delta = 23.9, 28.9, 39.0, 39.3, 43.7, 50.9, 53.2, 110.7, 134.7, 136.7, 144.3, 162.8, 212.7; \ [\alpha]_{20}^D = -34.0 ^\circ (c \ 1.00 \text{ CHCl}_3); \text{HPLC (OB–H, 2% i-PrOH in hexane, 0.5 mL/min, 230 nm): t} \text{major} = 35.5 \text{ min, t} \text{minor} = 49.2 \text{ min, 93% ee; HR–MS (EI): calcd for C}_{13}\text{H}_{17}\text{NO}_2 (M) 219.1259 found 219.1257.}

(S)-3-(6-methoxy-3-pyridyl)-nonan-2-one (3d)
IR (neat) \(\nu = 2927, 1714, 1491, 1286, 1026, 828 \text{ cm}^{-1}\); \(^1\text{H} \text{NMR} (270 \text{ MHz, CDCl}_3) \delta = 0.83 (t, \(J = 6.7 \text{ Hz, 3H}), 1.08–1.23 (m, 6H), 1.47–1.61 (m, 2H), 2.04 (s, 3H), 2.70 (d, \(J = 4.0 \text{ Hz, 2H}), 3.03–3.11 (m, 1H), 3.91 (s, 3H), 6.69 (d, \(J = 8.4 \text{ Hz, 1H}), 7.39
(dd, J = 2.8, 8.4 Hz, 1H), 7.97 (d, J = 2.8 Hz, 1H); $^{13}$C NMR (67 MHz, CDCl$_3$) δ = 13.9, 22.4, 26.9, 30.6, 31.6, 36.2, 37.7, 50.6, 53.3, 110.7, 132.4, 137.6, 145.7, 162.9, 207.3; $[^\alpha]^{20}_D$ = -21.0° (c 1.00 CHCl$_3$); HPLC (OJ–H, 0.5% i-PrOH in hexane, 0.5 mL/min, 230 nm): $t_{\text{major}}$ = 23.3 min, $t_{\text{minor}}$ = 29.6 min, 91% ee; HR–MS (EI): calcd for C$_{11}$H$_{23}$NO$_2$ (M) 249.1729 found 249.1729.

(S)-i-Propyl-3-(6-methoxy-3-pyridyl)-butanoate (3e)
IR (neat) ν = 2978, 1726, 1493, 1328, 1106, 830 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) δ = 1.09 (d, J = 6.3 Hz, 3H), 1.13 (d, J = 6.3 Hz, 3H), 1.24 (d, J = 6.8 Hz, 3H), 2.47 (d, J = 7.8 Hz, 2H), 3.17–3.22 (m, 1H), 3.87 (s, 3H), 4.87–4.92 (m, 1H), 6.65 (d, J = 8.3 Hz, 1H), 7.40 (d, J = 8.3 Hz, 1H), 7.97 (s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ = 21.6, 21.7, 21.8, 33.4, 43.0, 53.2, 67.6, 110.5, 133.4, 137.1, 145.0, 162.9, 171.4; $[^\alpha]^{20}_D$ = -21.0° (c 1.00 CHCl$_3$); HPLC (OJ–H, 0.5% i-PrOH in hexane, 0.5 mL/min, 230 nm): $t_{\text{major}}$ = 15.9 min, $t_{\text{minor}}$ = 18.4 min, 82% ee; HR–MS (EI): calcd for C$_{13}$H$_{19}$NO$_3$ (M) 237.1365 found 237.1361.

(S)-3-(6-methoxy-3-pyridyl)-N-p-tolylbutanamide (3f)
IR (neat) ν = 2978, 1726, 1493, 1328, 1106, 830 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) δ = 1.35 (d, J = 7.3 Hz, 3H), 2.18 (s, 3H), 2.57 (d, J = 7.3 Hz, 2H), 3.35–3.41 (m, 1H), 3.91 (s, 3H), 6.69 (d, J = 8.3 Hz, 1H), 7.09 (t, J = 7.3 Hz, 1H), 7.18 (br, 1H), 7.27–7.31 (m, 1H), 7.41–7.49 (m, 3H), 8.07 (br, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ = 21.5, 30.9, 33.6, 46.4, 53.4, 110.7, 119.9, 124.4, 129.0, 133.5, 137.4, 137.6, 144.9, 160.6, 169.4; $[^\alpha]^{20}_D$ = -31.0° (c 1.00 CHCl$_3$); HPLC (AD–H, 10% i-PrOH in hexane, 0.5 mL/min, 230 nm): $t_{\text{major}}$ = 39.3 min, $t_{\text{minor}}$ = 34.4 min, 76% ee; HR–MS (EI+$^+$): calcd for C$_{17}$H$_{20}$N$_2$O$_2$ (M$^+$) 284.1525 found 284.1511.

(R)-3-(6-methoxy-2-pyridyl)-cyclohexanone (3h)
IR (neat) ν = 2927, 1709, 1577, 1465, 1290, 799 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) δ = 1.79–2.06 (m, 4H), 2.40–2.42 (m, 2H), 2.56 (d, J = 10.8 Hz, 1H), 2.78 (t, J = 10.3 Hz, 1H), 3.15–3.19 (m, 1H), 3.89 (s, 3H), 6.58 (d, J = 8.3 Hz, 1H), 6.70 (d, J = 7.3 Hz, 1H), 7.48 (dd, J = 7.3, 8.4 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ = 24.5, 30.9, 33.6, 46.4, 53.4, 110.7, 119.9, 124.4, 129.0, 133.5, 137.4, 137.6, 144.9, 160.6, 163.0, 169.4; $[^\alpha]^{20}_D$ = -7.6° (c 1.00 CHCl$_3$); HPLC (AD–H, 1% i-PrOH in hexane, 0.5 mL/min, 230 nm): $t_{\text{major}}$ = 26.1 min, $t_{\text{minor}}$ = 24.8 min, 93% ee; HR–MS (EI): calcd for C$_{12}$H$_{15}$NO$_2$ (M) 205.1103 found 205.1108.

(R)-3-(6-methoxy-2-pyridyl)-nonan-2-one (3i)
IR (neat) ν = 2928, 1716, 1578, 1464, 1288, 800 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) δ = 0.83 (t, J = 6.8 Hz, 3H), 1.09–1.25 (m, 6H), 1.50–1.56 (m, 1H), 1.67–1.72 (m, 1H), 2.16 (s, 3H), 2.65 (dd, J = 5.6, 16.8 Hz, 1H), 3.05 (dd, J = 8.4, 16.8 Hz, 1H), 3.16–3.22 (m, 1H), 3.89 (s, 3H), 6.52 (d, J = 8.0 Hz, 1H), 6.72 (d, J = 6.4 Hz, 1H), 7.45 (dd, J = 6.4, 8.0 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ = 13.5, 22.0, 26.4, 30.0, 31.3, 34.7, 41.7, 48.0, 52.5, 107.1, 115.3, 138.1, 160.8, 163.2, 207.9; $[^\alpha]^{20}_D$ = +1.5° (c 1.00 CHCl$_3$); HPLC (OB-H, 0.25% i-PrOH in hexane, 0.5 mL/min, 230 nm): $t_{\text{major}}$ = 36.7 min, $t_{\text{minor}}$ = 32.9 min, 81% ee; HR–MS (EI): calcd for C$_{15}$H$_{25}$NO$_2$ (M)
249.1729 found 249.1730.

(S)-3-(5-Methoxy-2-thienyl)-cyclohexanone (3n)
IR (neat) ν = 2939, 1708, 1560, 1508, 1201, 768 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ = 1.73–1.81 (m, 2H), 2.08–2.19 (m, 2H), 2.33–2.52 (m, 3H), 2.69 (dt, J = 13.7, 1.9 Hz, 1H), 3.15–3.16 (m, 1H), 3.85 (s, 3H), 5.99 (d, J = 3.9 Hz, 1H), 6.41 (d, J = 3.9 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ = 24.7, 33.5, 39.9, 41.1, 49.0, 60.2, 102.8, 119.9, 134.3, 164.5, 210.2; [α]²⁰D = -28.4° (c 1.00 CHCl₃); HPLC (AD–H, 0.5% i-PrOH in hexane, 0.5 mL/min, 230 nm): t_major = 33.5 min, t_minor = 30.0 min, 90% ee; HR–MS (EI): calcd for C₁₂H₁₅NO₂ (M) 210.0715 found 210.0714.

(S)-3-(5-Methoxy-2-thienyl)-nonan-2-one (3o)
IR (neat) ν = 2927, 1715, 1509, 1356, 1207, 767 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ = 0.85 (t, J = 6.8 Hz, 3H), 1.24 (br, 6H), 1.46–1.56 (m, 2H), 2.07 (s, 3H), 2.62 (dd, J = 6.4, 16.1 Hz, 1H), 2.71 (dd, J = 7.3, 16.1 Hz, 1H), 3.25 (tt, J = 5.1, 7.3 Hz, 1H), 3.84 (s, 3H), 5.94 (d, J = 3.9 Hz, 1H), 6.37 (dd, J = 3.9 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ = 14.0, 22.5, 26.9, 30.7, 31.6, 37.1, 37.2, 51.4, 60.1, 102.5, 121.1, 134.6, 164.1, 207.7; [α]²⁰D = -23.5° (c 1.00 CHCl₃); HPLC (AD–H, 0.5% i-PrOH in hexane, 0.5 mL/min, 230 nm): t_major = 35.3 min, t_minor = 29.5 min, 88% ee; HR–MS (EI): calcd for C₁₄H₂₂O₂S (M) 254.1341 found 254.1341.

3d
ONMe

3h