

Supporting Information

Triethylborane-Induced Radical Allylation Reaction with Zirconocene-Olefin Comolex
(0L036431E)

Koji Hirano, Kazuya Fujita, Hiroshi Shinokubo, and Koichiro Oshima*

*Department of Material Chemistry, Graduate School of Engineering, Kyoto University,
Kyoto-daigaku Katsura, Nishikyo-ku, Kyoto 615-8510, Japan*

Instrumentation and Materials

^1H NMR (300 MHz) and ^{13}C NMR (75.3 MHz) spectra were taken on Varian GEMINI 300 and Mercury 300 spectrometers. ^1H NMR and ^{13}C NMR spectra were obtained in CDCl_3 with tetramethylsilane as an internal standard. IR spectra were determined on a SHIMADZU FTIR-8200PC spectrometer. Mass spectra were determined on a JEOL Mstation 700 spectrometer. TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel 60F₂₅₄. Silica gel (Wakogel 200 mesh) was used for column chromatography. The analyses were carried out at the Elemental Analysis Center of Kyoto University.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Tetrahydrofuran (THF) was freshly distilled from sodium benzophenone ketyl before use. Benzene was dried over slices of sodium. Cp_2ZrCl_2 was purchased from TCI and was used as received. Et_3B was purchased from Aldrich Chemicals and was diluted to prepare a 1.0 M hexane solution, which was stored strictly under argon.

Experimental Section

General Procedure for Reaction of Allylzirconium Reagent with α -Iodo Carbonyl Compound

THF (10 mL) and Cp_2ZrCl_2 (878 mg, 3.0 mmol) were placed in a 50-mL reaction flask under argon. After the mixture was cooled to $-78\text{ }^\circ\text{C}$ in a dry ice bath, allylmagnesium chloride (3.0 mL, 1.0 M THF solution, 3.0 mmol) was added dropwise and stirred for 30 min at the same temperature. To the reaction mixture was added a solution of benzyl iodoacetate (**2a**, 276 mg, 1.0 mmol) and triethylborane (0.2 mL, 1.0 M hexane solution, 0.2 mmol) at $-78\text{ }^\circ\text{C}$ and the temperature was raised to ambient temperature. After being stirred at $25\text{ }^\circ\text{C}$ for additional 1 h, the mixture was poured into hydrochloric acid (20 mL, 1 M). Extraction with hexane/ethyl acetate (5/1, 25 mL \times 3) followed by silica gel column purification afforded benzyl 4-pentenoate (**3a**, 177 mg, 0.93 mmol) in 93% yield.

General Procedure with α -Bromo Carbonyl Compound

Under an argon atmosphere, to a solution of Cp_2ZrCl_2 (878 mg, 3.0 mmol) in THF (10 mL) was added a solution of allylmagnesium chloride (3.0 mL, 1.0 M THF solution, 3.0 mmol) at $-78\text{ }^\circ\text{C}$. A solution of *N,N*-diethyl bromoacetoamide (**2k**, 194 mg, 1.0 mmol) and triethylborane (1.0 mL, 1.0 M hexane solution, 1.0 mmol) was then added dropwise to the reaction mixture at $-78\text{ }^\circ\text{C}$ and the resultant solution was stirred at ambient temperature. After quenching the reaction mixture by 1 M HCl, the mixture was extracted by hexane/ethyl acetate (5/1, 25 mL \times 3). The usual work up and purification by column chromatography on silica gel provided *N,N*-diethyl 4-pentenamide (**3k**, 149 mg, 0.96 mmol) in 96% yield.

Typical Procedure for Three Component Coupling

THF (10 mL) was added to Cp_2ZrCl_2 (878 mg, 3.0 mmol) in a 50-mL flask under argon. After the mixture was cooled to $-78\text{ }^\circ\text{C}$, allylmagnesium chloride (3.0 mL, 1.0 M THF solution, 3.0 mmol) was added, and the resulting mixture was stirred for 30 min at the same temperature. A solution of iodocyclohexane (1.05 g, 5.0 mmol), acrylic acid *tert*-butyl ester (128 mg, 1.0 mmol) and triethylborane (0.2 mL, 1.0 M hexane solution, 0.2 mmol) was added to the reaction mixture. The mixture was warmed to room temperature over 4 h and then stirred for another 1 h at $25\text{ }^\circ\text{C}$. Quenching the reaction with aqueous HCl (20 mL, 1M) followed by extraction, concentration, and silica gel column purification yielded *tert*-butyl 2-cyclohexylmethyl-4-pentenoate (**7a**, 212 mg, 0.84 mmol) in 84% yield.

Typical Procedure for the Allylation Reaction with Zirconocene-Olefin Complex

Propylmagnesium bromide (6.0 mL, 1.0 M THF solution, 6.0 mmol) was added dropwise to a solution of Cp_2ZrCl_2 (878 mg, 3.0 mmol) in benzene (23 mL) at $0\text{ }^\circ\text{C}$, and the mixture was stirred at the same temperature for 30 min. To the reaction mixture was added a solution of diisopropyl ketone (514 mg, 4.5 mmol) in benzene (2 mL) at $0\text{ }^\circ\text{C}$. After being stirred for 3 h at $0\text{ }^\circ\text{C}$, benzyl iodoacetate (**2a**, 276 mg, 1.0 mmol) and triethylborane (0.2 mL, 1.0 M hexane solution, 0.2 mmol) was added to the resulting mixture at $0\text{ }^\circ\text{C}$ and the temperature was raised to ambient temperature. After being stirred at $25\text{ }^\circ\text{C}$ for additional 1 h, the mixture was poured into hydrochloric acid (20 mL, 1 M). Extraction with hexane/ethyl acetate (5/1, 25 mL \times 3) followed by silica gel column purification furnished benzyl 4-pentenoate (**3a**, 177 mg, 0.93 mmol) in 93% yield.

General Procedure for Crotylation Reaction with Zirconocene-Olefin Complex

To a stirred solution of Cp_2ZrCl_2 (878 mg, 3.0 mmol) in benzene (20 mL), butylmagnesium

bromide (6.0 mL, 1.0 M THF solution, 6.0 mmol) was added at 0 °C. After stirred for 30 min, the resulting solution was treated with diisopropyl ketone (514 mg, 4.5 mmol) in benzene (2 mL) at 0 °C. After being stirred for 3 h at 0 °C, benzyl iodoacetate (**2a**, 276 mg, 1.0 mmol) and triethylborane (0.2 mL, 1.0 M hexane solution, 0.2 mmol) was added dropwise to the reaction mixture at the same temperature and the reaction temperature was gradually raised to room temperature. After being stirred at 25 °C for additional 1 h, the mixture was quenched with hydrochloric acid (20 mL, 1 M). The mixture was extracted with hexane/ethyl acetate (5/1, 25 mL × 3) and combined organic extracts were dried over anhydrous Na₂SO₄, and concentrated in vacuo. The crude product was purified by column chromatography to afford benzyl 3-methyl-4-pentenoate (**15a**, 202 mg, 0.99 mmol) in 99% yield.

Characterization Data

Spectral data for some compounds (**3a**¹, **3b**¹, **3c**², **3e**³, **3f**⁴, **3g**⁵, **7b**⁶,) were found in the literatures.

6-Chlorohexyl 4-Pentenoate (3d): IR (neat) 3080, 2937, 2862, 1738, 1641, 1447, 1390, 1352, 1256, 1175, 1105, 997, 916, 731, 650 cm⁻¹; ¹H NMR (CDCl₃) δ 1.29–1.49 (m, 4H), 1.56–1.66 (m, 2H), 1.70–1.80 (m, 2H), 2.29–2.42 (m, 4H), 3.51 (t, *J* = 6.6 Hz, 2H), 4.05 (t, *J* = 6.6 Hz, 2H), 4.94–5.08 (m, 2H), 5.72–5.87 (m, 1H); ¹³C NMR (CDCl₃) δ 25.15, 26.36, 28.36, 28.77, 32.32, 33.44, 44.83, 64.20, 115.49, 136.78, 173.26. Found: C, 60.12; H, 8.84%. Calcd for C₁₁H₁₉ClO₂: C, 60.41; H, 8.76%.

Ethyl 2-(2-Propenyl)octanoate (3i): IR (neat) 3078, 2928, 1734, 1641, 1447, 1377, 1177, 1140, 1040, 993, 914, 856, 725 cm⁻¹; ¹H NMR (CDCl₃) δ 0.88 (t, *J* = 6.9 Hz, 3H), 1.23–1.27 (m, 13H), 2.19–2.26 (m, 1H), 2.30–2.35 (m, 1H), 2.38–2.44 (m, 1H), 4.13 (q, *J* =

7.2 Hz, 2H), 4.98–5.07 (m, 2H), 5.67–5.81 (m, 1H); ^{13}C NMR (CDCl_3) δ 14.04, 14.33, 22.56, 27.21, 29.15, 31.65, 31.86, 36.52, 45.37, 60.06, 116.52, 135.65, 175.76. HRMS Found: m/z 212.1778. Calcd for $\text{C}_{13}\text{H}_{24}\text{O}$: 212.1776.

Heptyl 2,2-dimethyl-4-pentenoate (3l): IR (neat) 3443, 3078, 2930, 2858, 1732, 1641, 1470, 1416, 1389, 1366, 1302, 1252, 1211, 1150, 1090, 995, 916, 864, 770, 725 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.88 (t, J = 6.6 Hz, 3H), 1.17 (s, 6H), 1.23–1.31 (m, 8H), 1.56–1.64 (m, 2H), 2.27 (d, J = 7.5 Hz, 2H), 4.04 (t, J = 6.6 Hz, 2H), 5.01–5.06 (m, 2H), 5.66–5.80 (m, 1H); ^{13}C NMR (CDCl_3) δ 19.12, 22.02, 24.92, 26.00, 28.59, 28.71, 28.97, 44.34, 44.80, 64.54, 117.70, 134.23, 177.38. Found: C, 74.07; H, 11.68%. Calcd for $\text{C}_{14}\text{H}_{26}\text{O}$: C, 74.29; H, 11.58%.

***tert*-Butyl 2-(cyclohexylmethyl)-4-pentenoate (7a):** IR (neat) 3078, 2924, 2853, 1728, 1641, 1448, 1391, 1367, 1151, 978, 914, 847 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.86–0.88 (m, 2H), 1.17–1.26 (m, 6H), 1.44 (s, 9H), 1.62–1.66 (m, 4H), 1.78–1.82 (m, 1H), 2.08–2.18 (m, 1H), 2.24–2.33 (m, 1H), 2.37–2.45 (m, 1H), 4.98–5.07 (m, 2H), 5.67–5.81 (m, 1H); ^{13}C NMR (CDCl_3) δ 26.40, 28.22, 32.86, 33.82, 35.73, 37.35, 39.90, 43.49, 79.96, 116.21, 135.75, 175.13. HRMS Found: m/z 252.2098. Calcd for $\text{C}_{13}\text{H}_{24}\text{O}$: 252.2096.

Benzyl 3-Methyl-4-pentenoate (15a): IR (neat) 3069, 3034, 2932, 2963, 2874, 1783, 1641, 1499, 1456, 1418, 1379, 1352, 1171, 1103, 997, 916, 739, 698 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.03 (d, J = 6.9 Hz, 3H), 2.26–2.44 (m, 2H), 2.64–2.74 (m, 1H), 4.93 (d, J = 10.5 Hz, 1H), 4.98 (d, J = 17.1 Hz, 1H), 5.10 (s, 2H), 5.75 (ddd, J = 7.2, 10.5, 17.1 Hz, 1H), 7.26–7.37 (m, 5H); ^{13}C NMR (CDCl_3) δ 19.60, 34.35, 41.20, 66.11, 113.48, 128.27, 128.33, 128.60, 136.09, 142.47, 172.49. Found: C, 76.23; H, 8.02%. Calcd for $\text{C}_{13}\text{H}_{16}\text{O}_2$: C, 76.44; H,

7.90%.

***N,N*-Diethyl 3-methyl-4-pentanamide (15b):** IR (neat) 3475, 3080, 2972, 2933, 2875, 1643, 1431, 1380, 1363, 1276, 1251, 1222, 1137, 1082, 997, 912, 732, 416 cm⁻¹; ¹H NMR (CDCl₃) δ 1.05–1.18 (m, 6H), 2.22 (dd, *J* = 7.8, 15.0 Hz, 1H), 2.34 (dd, *J* = 6.6, 15.0 Hz, 1H), 2.75–2.84 (m, 1H), 3.26–3.41 (m, 4H), 4.92–5.06 (m, 2H), 5.83 (ddd, *J* = 6.9, 9.9, 16.8 Hz, 1H); ¹³C NMR (CDCl₃) δ 13.25, 14.59, 19.66, 34.49, 39.72, 40.21, 42.21, 112.73, 143.20, 170.74. HRMS Found: *m/z* 169.1461. Calcd for C₁₃H₂₄O: 169.1467.

References and Notes

- (1) Kohno, Y.; Narasaka, K. *Bull. Chem. Soc. Jpn.* **1995**, 68, 322.
- (2) Hirao, T.; Fujii, T.; Ohshiro, Y. *Tetrahedron* **1994**, 50, 10207.
- (3) Patton, J. T.; Boncella, J. M.; Wagener, K. P. *Macromolecules* **1992**, 25, 3862.
- (4) Maligres, P. E.; Weissman, S. A.; Upadhyay, V.; Cianciosi, S. J.; Reamer, R. A.; Purick, R. M.; Sager, J.; Rossen, K.; Eng, K. K.; Askin, D.; Valonte, R.P.; Reider, P. J. *Tetrahedron* **1996**, 52, 3327.
- (5) Martin-Lopez, M. J.; Bermegjo, F. *Tetrahedron* **1998**, 54, 12379.
- (6) Casimir, J. R.; Ettouati, L.; Paris, J. *Letters in Peptide Science* **1998**, 5, 13.