Supporting Information

Nickel-Catalyzed 1,4-Addition of Trialkylboranes to α,β -Unsaturated Esters: Dramatic Enhancement by Addition of Methanol

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Instrumentation and Chemicals

^1H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were taken on Varian UNITY INOVA 500 spectrometers and were recorded in CDCl_3 . Chemical shifts (δ) are in parts per million relative to tetramethylsilane at 0.00 ppm for ^1H and relative to CDCl_3 at 77.0 ppm for ^{13}C unless otherwise noted. IR spectra were determined on a SHIMADZU FTIR-8200PC 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. Elemental 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. Toluene was stored over slices of sodium. Triethylborane, tributylborane, and 9-borabicyclo[3.3.1]nonane (9-BBN) dimer were purchased from Aldrich. Tri(*tert*-butyl)phosphine was obtained from Wako Pure Chemical Co. Triethylborane and tri(*tert*-butyl)phosphine were diluted to prepare 1.0 M hexane solutions, which were stored strictly under argon. Bis(1,5-cyclooctadiene)nickel was available from Strem. All reactions were carried out under argon atmosphere.

Typical Procedure for the Nickel-Catalyzed 1,4-Addition of Trialkylboranes to α,β -Unsaturated Esters

Synthesis of 3a: With a glovebox filled with argon, Ni(cod)₂ (11 mg, 0.04 mmol) and Cs₂CO₃ (489 mg, 1.5 mmol) were placed in a reaction flask. Toluene (3 mL) and P(*t*-Bu)₃ (purchased from Wako and diluted to prepare a degassed hexane solution, 1.0 M, 0.096 mL, 0.096 mmol) were added dropwise. The suspension was stirred for 10 min at 0 °C. A solution of benzyl (*E*)-crotonate (**1a**, 88 mg, 0.5 mmol) in toluene (2 mL) and Et₃B (1.0 M hexane solution, 1.5 mL, 1.5 mmol) were then added. The mixture was allowed to warm to room temperature and stirred for 17 h. The resulting mixture was poured into 1.0 M hydrochloric acid (10 mL). The product was extracted with hexane/ethyl acetate (20:1). The combined organic layer was dried over sodium sulfate, and concentrated in vacuo. Silica gel column purification (hexane : ethyl acetate = 40 : 1) gave benzyl 3-methylpentanoate (**3a**, 91 mg, 0.44 mmol) in 88% yield.

Synthesis of 8a: With a glovebox filled with argon, 9-BBN dimer (commercially available from Aldrich, 183 mg, 1.5 mmol) was placed in a reaction flask. A solution of benzyl 11-undecenyl ether (**6a**, 469 mg, 1.8 mmol) in THF (3 mL) was added dropwise. The solution was stirred for 15 h at room temperature to prepare alkylborane **7a**. On the other hand, with a glovebox filled with argon, Ni(cod)₂ (11 mg, 0.04 mmol) and Cs₂CO₃ (489 mg, 1.5 mmol) were placed in another reaction flask. Toluene (3 mL) and P(*t*-Bu)₃ (1.0 M, 0.096 mL, 0.096 mmol) were added dropwise. The suspension was stirred for 10 min at 0 °C. Methanol (0.081 mL, 2.0 mmol) was added to **7a** prepared in advance and the solution was then transferred to the mixture of nickel catalysis and Cs₂CO₃ in toluene *via* a syringe under argon. Finally, a solution of benzyl (*E*)-crotonate (**1a**, 88 mg, 0.5 mmol) in toluene (2 mL) was added. After being stirred for 8.5 h at room temperature, the resulting mixture was poured into 1.0 M hydrochloric acid (10 mL). Extraction with hexane/ethyl acetate (20:1) followed by silica gel column purification afforded benzyl 14-benzyloxy-3-methyltetradecanoate (**8a**, 210 mg, 0.48 mmol) in 96% yield.

Characterization Data for Compounds

¹H NMR spectra for known compounds **3c**, **3d**, **3g**, **5a**, and **5b** are attached in the last part.

Benzyl 3-methylpentanoate (3a): IR (neat) 3035, 2963, 2932, 2858, 1734, 1499, 1456, 1381, 1155, 1097, 981, 738, 697 cm⁻¹; ¹H NMR (CDCl₃) δ 0.90 (t, *J* = 7.5 Hz, 3H), 0.94 (d, *J* = 6.5 Hz, 3H), 1.19–1.28 (m, 1H), 1.33–1.41 (m, 1H), 1.87–1.97 (m, 1H), 2.17 (dd, *J* = 8.0, 15.0 Hz, 1H), 2.38 (dd, *J* = 6.0, 15.0 Hz, 1H), 5.13 (s, 2H), 7.32–7.40 (m, 5H); ¹³C NMR (CDCl₃) δ 11.25, 19.25, 29.30, 31.93, 41.45, 66.00, 128.13, 128.16, 128.51, 136.11, 173.23. Found: C, 75.90; H, 8.72%. Calcd for C₁₃H₁₈O₂: C, 75.96; H, 8.80%.

***p*-Chlorobenzyl 3-methylpentanoate (3b):** IR (neat) 2932, 2857, 1733, 1495, 1456, 1411, 1381, 1241, 1155, 1094, 1016, 982, 807 cm⁻¹; ¹H NMR (CDCl₃) δ 0.89 (t, *J* = 7.5 Hz, 3H), 0.93 (d, *J* = 6.5 Hz, 3H), 1.19–1.28 (m, 1H), 1.32–1.42 (m, 1H), 1.86–1.85 (m, 1H), 2.16 (dd, *J* = 15.0, 8.0 Hz, 1H), 2.37 (dd, *J* = 15.0, 6.0 Hz, 1H), 5.08 (s, 2H), 7.30 (d, *J* = 8.5 Hz, 2H), 7.34 (d, *J* = 8.5 Hz, 2H); ¹³C NMR (CDCl₃) δ 11.23, 19.25, 29.29, 31.93, 41.38, 65.14, 128.70, 129.56, 134.02, 134.65, 173.06. Found: C, 64.84; H, 7.31%. Calcd for C₁₃H₁₇ClO₂: C, 64.86; H, 7.12%.

***p*-Chlorobenzyl 3-methylheptanoate (3h):** IR (neat) 2930, 2859, 1733, 1495, 1456, 1379, 1214, 1169, 1095, 806 cm⁻¹; ¹H NMR (CDCl₃) δ 0.88 (t, *J* = 7.0 Hz, 3H), 0.93 (d, *J* = 7.0 Hz, 3H), 1.16–1.32 (m, 6H), 1.94–1.99 (m, 1H), 2.16 (dd, *J* = 15.0, 8.0 Hz, 1H), 2.34 (dd, *J* = 15.0, 6.0 Hz, 1H), 5.08 (s, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H); ¹³C NMR (CDCl₃) δ 14.01, 19.71, 22.74, 29.05, 30.35, 36.33, 41.78, 65.12, 128.68, 129.58, 134.02, 134.66, 173.03. Found: C, 67.31; H, 7.99%. Calcd for C₁₅H₂₁ClO₂: C, 67.03; H, 7.88%.

Ethyl 3-(2-phenylethyl)heptanoate (3i): IR (neat) 3027, 2930, 2859, 1733, 1604, 1496, 1456, 1373, 1157, 1100, 1033, 747, 699 cm⁻¹; ¹H NMR (CDCl₃) δ 0.91 (t, *J* = 7.5 Hz, 3H), 1.24–1.44 (m, 6H), 1.27 (t, *J* = 7.0 Hz, 3H), 1.59–1.69 (m, 2H), 1.91–1.98 (m, 1H), 2.31 (d, *J* = 6.5 Hz, 2H), 2.62 (t, *J* = 8.0 Hz, 2H), 4.14 (q, *J* = 7.0 Hz, 2H), 7.17–7.20 (m, 2H), 7.27–7.30 (m, 3H); ¹³C NMR (CDCl₃) δ 14.03, 14.25, 22.87, 28.62, 32.96, 33.40, 34.83, 35.82, 39.12, 60.13, 125.67, 128.28, 128.29, 142.55, 173.37. Found: C, 77.82; H, 10.21%. Calcd for C₁₇H₂₆O₂: C, 77.82; H, 9.99%.

Ethyl 3-cyclohexylheptanoate (3j): IR (neat) 2926, 2854, 1739, 1449, 1369, 1312, 1277, 1246, 1213, 1161, 1133, 1097, 1037 cm⁻¹; ¹H NMR (CDCl₃) δ 0.89 (t, *J* = 7.5 Hz, 3H), 0.94–1.05 (m, 2H), 1.06–1.16 (m, 1H), 1.16–1.39 (m, 9H), 1.26 (t, *J* = 7.5 Hz, 3H), 1.60–1.68 (m, 3H), 1.73–1.79 (m, 3H), 2.15 (dd, *J* = 15.0, 7.5 Hz, 1H), 2.31 (dd, *J* = 15.0, 6.5 Hz, 1H), 4.13 (q, *J* = 7.5 Hz, 2H); ¹³C NMR (CDCl₃) δ 14.05, 14.24, 22.94, 26.72, 26.76, 26.80, 29.13, 29.48, 29.95, 30.90, 36.60, 40.36, 40.52, 60.05, 174.25. Found: C, 74.89; H, 11.97%. Calcd for C₁₅H₂₈O₂: C, 74.95; H, 11.74%.

Benzyl 14-benzyloxy-3-methyltetradecanoate (8a): IR (neat) 3033, 2927, 2855, 1733, 1498, 1456, 1380, 1362, 1259, 1168, 1103, 1029, 1002, 735, 697 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.94 (d, $J = 6.5$ Hz, 3H), 1.18–1.39 (m, 18H), 1.60–1.66 (m, 2H), 1.96–2.00 (m, 1H), 2.18 (dd, $J = 15.0, 8.0$ Hz, 1H), 2.36 (dd, $J = 15.0, 6.0$ Hz, 1H), 3.48 (t, $J = 7.0$ Hz, 2H), 4.52 (s, 2H), 5.13 (s, 2H), 7.27–7.39 (m, 10H); ^{13}C NMR (CDCl_3) δ 19.74, 26.19, 26.88, 29.47, 29.59 (Four signals were overlapped), 29.74, 29.77, 30.40, 36.71, 41.86, 65.97, 70.54, 72.84, 127.42, 127.59, 128.11, 128.17, 128.31, 128.50, 136.19, 138.75, 173.15. Found: C, 79.63; H, 9.61%. Calcd for $\text{C}_{29}\text{H}_{42}\text{O}_3$: C, 79.41; H, 9.65%.

Benzyl 3-methylnonanoate (8b): IR (neat) 3035, 2928, 2856, 2360, 1733, 1699, 1499, 1456, 1379, 1167, 1111, 1081, 1003, 736, 697 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.89 (t, $J = 7.0$ Hz, 3H), 0.94 (d, $J = 6.5$ Hz, 3H), 1.16–1.31 (m, 10H), 1.97–2.00 (m, 1H), 2.18 (dd, $J = 14.5, 8.0$ Hz, 1H), 2.36 (dd, $J = 14.5, 6.0$ Hz, 1H), 5.13 (s, 2H), 7.32–7.40 (m, 5H); ^{13}C NMR (CDCl_3) δ 14.06, 19.74, 22.62, 26.83, 29.40, 30.41, 31.81, 36.71, 41.88, 65.98, 128.12, 128.18, 128.51, 136.19, 173.16. Found: C, 77.60; H, 9.80%. Calcd for $\text{C}_{17}\text{H}_{26}\text{O}_2$: C, 77.82; H, 9.99%.

Benzyl 3-methyl-7-phenylheptanoate (8c): IR (neat) 3064, 3028, 2931, 2856, 1733, 1497, 1454, 1381, 1356, 1148, 1091, 1030, 982, 748, 698 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.93 (d, $J = 6.5$ Hz, 3H), 1.18–1.26 (m, 1H), 1.28–1.43 (m, 3H), 1.56–1.63 (m, 2H), 1.95–2.02 (m, 1H), 2.18 (dd, $J = 14.5, 8.0$ Hz, 1H), 2.35 (d, $J = 14.5, 6.0$ Hz, 1H), 2.60 (t, $J = 7.5$ Hz, 2H), 5.13 (s, 2H), 7.17–7.20 (m, 3H), 7.27–7.30 (m, 2H), 7.32–7.39 (m, 5H); ^{13}C NMR (CDCl_3) δ 19.73, 26.54, 30.34, 31.52, 35.86, 36.48, 41.84, 66.01, 125.60, 128.15, 128.21, 128.23, 128.37, 128.52, 136.14, 142.67, 173.09. Found: C, 81.49; H, 8.69%. Calcd for $\text{C}_{21}\text{H}_{26}\text{O}_2$: C, 81.25; H, 8.44%.

Benzyl 5-ethyl-3-methylheptanoate (8d): IR (neat) 2962, 2921, 2874, 1738, 1457, 1382, 1216, 1168, 1125, 697 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.82 (t, $J = 7.0$ Hz, 3H), 0.84 (t, $J = 7.0$ Hz, 3H), 0.93 (d, $J = 6.5$ Hz, 3H), 1.06–1.12 (m, 1H), 1.16–1.36 (m, 6H), 2.01–2.11 (m, 1H), 2.17 (dd, $J = 14.5, 8.0$ Hz, 1H), 2.34 (dd, $J = 14.5, 6.0$ Hz, 1H), 5.13 (s, 2H), 7.32–7.40 (m, 5H); ^{13}C NMR (CDCl_3) δ 10.36, 10.78, 20.02, 24.97, 25.74, 27.96, 37.47, 40.53, 42.30, 65.99, 128.13, 128.23, 128.50, 136.18, 173.11. Found: C, 77.81; H, 10.24%. Calcd for $\text{C}_{17}\text{H}_{26}\text{O}_2$: C, 77.82; H, 9.99%.

Benzyl 3,6,6-trimethylheptanoate (8e): IR (neat) 3035, 2935, 2867, 1738, 1499, 1456, 1381, 1365, 1301, 1247, 1146, 1085, 982, 737, 697 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.85 (s, 9H), 0.94 (d, $J = 7.0$ Hz, 3H), 1.10–1.31 (m, 4H), 1.88–1.95 (m, 1H), 2.18 (dd, $J = 14.5, 8.0$ Hz, 1H), 2.38 (dd, $J = 14.5, 6.0$ Hz, 1H), 5.13 (s, 2H), 7.31–7.39 (m, 5H); ^{13}C NMR (CDCl_3) δ 19.83, 29.32, 30.14, 31.13, 31.41, 41.15, 41.88, 65.99, 128.14, 128.21, 128.53, 136.18, 173.15. Found: C, 77.93; H, 10.13%. Calcd for $\text{C}_{17}\text{H}_{26}\text{O}_2$: C, 77.82; H, 9.99%.

Benzyl 6-(dimethylphenylsilyl)-3-methylhexanoate (8f): IR (neat) 2960, 2935, 2874, 1734, 1449, 1371, 1178, 1081, 994, 947, 748, 692 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.26 (s, 6H), 0.66–0.77 (m, 2H), 0.90 (d, $J = 6.5$ Hz, 3H), 1.20–1.25 (m, 1H), 1.27–1.39 (m, 3H), 1.95–2.02 (m, 1H), 2.15 (dd, $J = 15.0$, 8.0 Hz, 1H), 2.32 (dd, $J = 15.0$, 6.0 Hz, 1H), 5.12 (s, 2H), 7.34–7.38 (m, 8H), 7.49–7.53 (m, 2H); ^{13}C NMR (CDCl_3) δ –3.04, 15.70, 19.63, 21.15, 30.04, 40.60, 41.82, 65.98, 127.71, 128.13, 128.19, 128.51, 128.77, 133.52, 136.17, 139.50, 173.10. Found: C, 74.53; H, 8.72%. Calcd for $\text{C}_{22}\text{H}_{30}\text{O}_2\text{Si}$: C, 74.53; H, 8.53%.

Benzyl 14-(*tert*-butyldimethylsiloxy)-3-methyltetradecanoate (8g): IR (neat) 2928, 2855, 1739, 1463, 1256, 1165, 1100, 1006, 836, 775, 696 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.06 (s, 6H), 0.91 (s, 9H), 0.94 (d, $J = 6.5$ Hz, 3H), 1.18–1.29 (m, 18H), 1.49–1.55 (m, 2H), 1.97–2.00 (m, 1H), 2.17 (dd, $J = 15.0$, 8.0 Hz, 1H), 2.36 (dd, $J = 15.0$, 6.0 Hz, 1H), 3.61 (t, $J = 6.5$ Hz, 2H), 5.13 (s, 2H), 7.31–7.39 (m, 5H); ^{13}C NMR (CDCl_3) δ –5.26, 18.37, 19.74, 25.81, 25.99, 26.89, 29.45, 29.61 (Three signals were overlapped), 29.64, 29.75, 30.42, 32.90, 36.73, 41.88, 63.34, 65.98, 128.12, 128.18, 128.51, 136.20, 173.16. Found: C, 72.38; H, 10.72%. Calcd for $\text{C}_{28}\text{H}_{50}\text{O}_3\text{Si}$: C, 72.67; H, 10.89%.

Benzyl 14-benzoyloxy-3-methyltetradecanoate (8h): IR (neat) 2927, 2855, 1720, 1452, 1314, 1275, 1176, 1113, 1070, 712, 697 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.93 (d, $J = 6.5$ Hz, 3H), 1.19–1.36 (m, 16H), 1.42–1.48 (m, 2H), 1.75–1.81 (m, 2H), 1.94–2.01 (m, 1H), 2.17 (dd, $J = 14.5$, 8.0 Hz, 1H), 2.36 (dd, $J = 14.5$, 6.0 Hz, 1H), 4.33 (t, $J = 6.5$ Hz, 2H), 5.13 (s, 2H), 7.31–7.39 (m, 5H), 7.44–7.47 (m, 2H), 7.55–7.58 (m, 1H), 8.05–8.07 (m, 2H); ^{13}C NMR (CDCl_3) δ 19.72, 26.01, 26.86, 28.70, 29.25, 29.49, 29.53, 29.56 (Two signals were overlapped), 29.71, 30.38, 36.69, 41.85, 65.11, 65.96, 128.10, 128.15, 128.27, 128.48, 129.50, 130.56, 132.73, 136.16, 166.66, 173.13. Found: C, 77.02; H, 9.12%. Calcd for $\text{C}_{29}\text{H}_{40}\text{O}_4$: C, 76.95; H, 8.91%.

Benzyl 8-bromo-3-methyloctanoate (8i): IR (neat) 2933, 2857, 1736, 1455, 1381, 1226, 1168, 1144, 982, 737, 697 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.94 (d, $J = 7.0$ Hz, 3H), 1.16–1.26 (m, 1H), 1.27–1.46 (m, 5H), 1.81–1.87 (m, 2H), 1.95–2.02 (m, 1H), 2.19 (dd, $J = 15.0$, 8.0 Hz, 1H), 2.35 (dd, $J = 15.0$, 6.0 Hz, 1H), 3.40 (t, $J = 7.0$ Hz, 2H), 5.13 (s, 2H), 7.32–7.40 (m, 5H); ^{13}C NMR (CDCl_3) δ 19.70, 26.02, 28.22, 30.28, 32.69, 33.81, 36.37, 41.78, 66.03, 128.17, 128.22, 128.53, 136.12, 172.99. Found: C, 58.85; H, 6.98%. Calcd for $\text{C}_{16}\text{H}_{23}\text{BrO}_2$: C, 58.72; H, 7.08%.

Figure S1. ^1H NMR spectrum of **3c** (B. H. Lipshutz, J. M. Serresko, B. R. Taft, *J. Am. Chem. Soc.* **2004**, *126*, 8352–8353.)

Figure S2. ^1H NMR spectrum of **3d** (F. López, S. R. Harutyunyan, A. Meetsma, A. J. Minnaard, B. L. Feringa, *Angew. Chem., Int. Ed.* **2005**, 44, 2752–2756.)

Figure S3. ^1H NMR spectrum of **3g** (M. Bergdahl, E.-L. Lindstedt, M. Nilsson, T. Olsson, *Tetrahedron* 1988, 44, 2055–2062.)

Figure S4. ^1H NMR spectrum of **5a** (T. Shintou, W. Kikuchi, T. Mukaiyama, *Bull. Chem. Soc. Jpn.* **2003**, 76, 1645–1667.)

Figure S5. ^1H NMR spectrum of **5b** (S. Ozaki, H. Matsushita, H. Ohmori, *J. Chem. Soc. Perkin Trans. 1*, 1993, 649–651.)