Nickel-Catalyzed Regioselective Three Component Coupling Reaction of Alkyl Halides, Butadienes, and Ar-M (M = MgX, ZnX)

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Supporting Information

Typical Experimental Procedures and Analytical Data of Products

2,3-Dimethyl-1-phenyl-2-octene (4a).

To a mixture of n-butyl bromide (205 mg, 1.5 mmol), 2,3-dimethyl-1,3-butadiene (82 mg, 1.0 mmol), and a catalytic amount of [(dppf)NiCl₂] (55 mg, 0.08 mmol) was added a THF solution of PhMgBr (1.0 M, 1.5 mL, 1.5 mmol) at 0 °C under nitrogen. After stirring for 24 h at 25 °C, 1 N HCl aq was added to the solution. A saturated aqueous NaHCO₃ solution (10 mL) was added, and the product was extracted with ether (10 mL). The organic layer was dried over MgSO₄, and evaporated to give a pale yellow crude product (78 % NMR yield). Purification by HPLC with CHCl₃ as an eluent afforded 149 mg (69 %) of 4a. IR (neat): 3083, 3026, 2927, 2858, 2729, 1602, 1453, 1260, 1211, 1151, 804 cm⁻¹, ¹H NMR (400 MHz, CDCl₃): (E isomer) δ = 7.28-7.25 (m, 2H), 7.29-7.14 (m, 3H), 3.39 (s, 2H), 2.08 (t, J = 7.6 Hz, 2H), 1.76 (s, 3H), 1.59 (s, 3H), 1.46-1.24 (m, 6H), 0.90 (t, J = 7.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): (E isomer) δ = 140.6, 130.1, 128.0, 127.8, 126.1, 125.2, 40.1, 34.5, 31.8, 27.8, 22.6, 18.5, 18.0, 14.1; ¹H NMR (400 MHz, CDCl₃): (Z
isomer) $\delta = 7.27-7.23$ (m, 2H), 7.17-7.13 (m, 3H), 3.40 (s, 2H), 2.13 (t, $J = 7.8$ Hz, 2H), 1.71 (s, 3H), 1.56 (s, 3H), 1.46-1.24 (m, 6H), 0.88 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): (Z isomer) $\delta = 140.9, 130.4, 128.4, 128.0, 126.1, 125.5, 39.7, 34.6, 32.0, 28.4, 22.7, 18.5, 18.4, 14.1; MS (EI) m/z (relative intensity, %) 216 (M$^+$, 47), 159 (13), 145 (100), 131 (17), 117 (43), 105 (8), 91(33), 83 (10), 69 (33), 55 (10), 41 (10); HR-MS: calcd for C$_{16}$H$_{24}$: 216.1878, found: 216.1875; elemental analysis: calcd for C$_{16}$H$_{24}$: C, 88.82; H, 11.18. found: C, 88.57; H, 11.02.

2,3,5,5-Tetramethyl-1-phenyl-2-hexene (4c).

To a mixture of $t$-butyl bromide (168 mg, 1.2 mmol), 2,3-dimethyl-1,3-butadiene (83 mg, 1.0 mmol), and a catalytic amount of [(dppf)NiCl$_2$] (54 mg, 0.08 mmol) was added a THF solution of PhMgBr (1.0 M, 1.5 mL, 1.5 mmol) at 0 °C under nitrogen. After stirring for 24 h at 25 °C, 1 N HClaq was added to the solution. Similar workup as mentioned above afforded a pale yellow crude product (80 % NMR yield). Purification by HPLC with CHCl$_3$ as an eluent afforded 161 mg (74 %) of 4c. IR (neat): 3083, 3026, 2865, 1602, 1476, 1466, 1380, 1320, 1234, 1178, 916, 862, 805 cm$^{-1}$, $^1$H NMR (400 MHz, CDCl$_3$): (E isomer) $\delta = 7.25-7.23$ (m, 2H), 7.17-7.12 (m, 3H), 3.42 (s, 2H), 2.10 (s, 2H), 1.82 (s, 3H), 1.60 (s, 3H), 0.95 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$): (E isomer) $\delta = 140.6, 129.6, 128.2, 127.8, 125.5, 125.3, 48.0, 40.5, 33.5, 29.6, 21.9, 19.6; $^1$H NMR (400 MHz, CDCl$_3$): (Z isomer) $\delta = 7.25-7.23$ (m, 2H), 7.17-7.12 (m, 3H), 3.42 (s, 2H), 2.18 (s, 2H), 1.76 (s, 3H), 1.55 (s, 3H), 0.95 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$): (Z isomer) $\delta = 140.5, 129.0, 128.0, 127.9, 125.5, 125.3, 47.8, 40.6, 33.1, 30.5, 21.8, 18.4; MS (EI) m/z (relative intensity, %) 216 (M$^+$, 43), 160 (78), 159 (25), 145 (100), 131 (14), 117 (56), 105 (8), 91(30), 65 (5), 57 (57), 41 (16), 29 (7); HR-MS: calcd for C$_{16}$H$_{24}$: 216.1878, found: 216.1874; elemental analysis: calcd for C$_{16}$H$_{24}$: C, 88.82; H, 11.18. found: C, 88.53; H, 11.23.
1-Cyclohexyl-2,3,4-triphenyl-2-butene (4d).

To a mixture of cyclohexyl bromide (198 mg, 1.2 mmol), 2,3-diphenyl-1,3-butadiene (206 mg, 1.0 mmol), and a catalytic amount of [(dppf)NiCl$_2$] (55 mg, 0.08 mmol) was added a THF solution of PhMgBr (1.0 M, 1.5 mL, 1.5 mmol) at 0 °C under nitrogen. After stirring for 24 h at 25 °C, 1 N HCl aq was added to the solution. Similar workup as mentioned above afforded a pale yellow crude product (81 % NMR yield). Purification by HPLC with CHCl$_3$ as an eluent afforded 267 mg (73 %) of 4d. IR (neat): 3057, 3024, 2922, 2850, 1599, 1493, 1442, 1069, 1029, 772 cm$^{-1}$, $^1$H NMR (400 MHz, CDCl$_3$): (E isomer) $\delta$ = 7.18-6.85 (m, 15H), 3.96 (s, 2H), 2.59 (d, $J$ = 7.2 Hz, 2H), 1.77-1.74 (m, 2H), 1.66-1.58 (m, 3H), 1.26-0.96 (m, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$): (E isomer) $\delta$ = 142.7, 142.6, 139.3, 138.6, 136.8, 129.7, 129.3, 128.2, 127.8, 127.0, 126.9, 125.4, 125.2, 125.1, 42.1, 40.4, 36.3, 33.3, 26.5, 26.3; $^1$H NMR (400 MHz, CDCl$_3$): (Z isomer) $\delta$ = 7.39-6.99 (m, 13H), 6.85 (d, $J$ = 6.8 Hz, 2H), 3.53 (s, 2H), 2.12 (d, $J$ = 6.8 Hz, 2H), 1.61-1.52 (m, 5H), 1.05-1.01 (m, 4H), 0.69-0.61 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): (Z isomer) $\delta$ = 142.2, 141.9, 139.6, 137.9, 137.2, 129.1, 128.6, 128.5, 127.8, 127.5, 127.3, 126.1, 125.7, 125.2, 42.8, 41.8, 35.4, 33.1, 26.4, 26.2. MS (EI) $m/z$ (relative intensity, %) 366 (M$^+$, 100), 269 (59), 205 (78), 191 (33), 178 (14), 167 (14), 115 (9), 103 (12), 91 (71), 55 (15), 41 (11); HR-MS: calcd for C$_{28}$H$_{30}$: 366.2347, found: 366.2365 elemental analysis: calcd for C$_{28}$H$_{30}$: C, 91.75; H, 8.25. found: C, 91.47; H, 8.30.

(E)-1-Cyclohexyl-1,4,4-triphenyl-2-butene (4e).

To a mixture of cyclohexyl bromide (815 mg, 5.0 mmol), 1,4-diphenyl-1,3-butadiene (412 mg, 2.0 mmol), and a catalytic amount of [(dppf)NiCl$_2$] (136 mg, 0.20 mmol) was added a THF solution of PhMgBr (1.0 M, 5.05 mL, 5.0 mmol) at 0 °C under nitrogen. After stirring for 48 h at 50 °C, 1 N HCl aq was added to the solution. Similar workup as mentioned above afforded a pale yellow crude product (72 % NMR yield). Purification by HPLC with CHCl$_3$ as an eluent afforded 440 mg (60 %) of 4e. IR (KBr) 2927, 2851, 1491, 1446, 761, 696 cm$^{-1}$; $^1$H NMR (400 MHz,
CDCl₃ δ 7.29-7.09 (m, 15 H), 5.90 (dd, J = 7.33, 15.26 Hz, 1 H), 5.58 (dd, J = 9.09, 15.26 Hz, 1 H), 4.70 (d, J = 7.33 Hz, 1 H), 3.01 (t, J = 9.09 Hz, 1 H), 1.85-1.39 (m, 5 H), 1.23-0.78 (m, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 144.2, 144.0, 143.9, 134.5, 132.8, 128.4, 128.3, 128.1, 128.0, 127.8, 125.9, 125.6, 56.2, 53.9, 42.7, 31.5, 31.4, 26.6, 26.5, 26.4; MS (EI) m/z (relative intensity, %) 366 (M⁺, 4), 283 (52), 205 (100), 193 (59), 167 (47), 115 (15), 91 (65); HRMS calcd for C₂₈H₃₀ 366.2348, found 366.2335; Anal. Calcd for C₂₈H₃₀: C, 91.75; H, 8.25. Found: C, 90.58; H, 8.20.

2,3,5-Trimethyl-1-phenyl-2-heptene (4f).

To a mixture of s-butyl chloride (112 mg, 1.2 mmol), 2,3-dimethyl-1,3-butadiene (86 mg, 1.0 mmol), and a catalytic amount of [(dppf)NiCl₂] (56 mg, 0.08 mmol) was added a THF solution of PhMgBr (1.0 M, 2.0 mL, 2.0 mmol) at 0 °C under nitrogen. After stirring for 24 h at 25 °C, 1 N HCl aq was added to the solution. Similar workup as mentioned above afforded a pale yellow crude product (66 % NMR yield). Purification by HPLC with CHCl₃ as an eluent afforded 143 mg (63 %) of 4f. IR (neat): 3084, 3026, 2874, 2729, 1602, 1494, 1375, 1189, 1153, 1123, 965, 918, 803 cm⁻¹, ¹H NMR (400 MHz, CDCl₃): (E isomer) δ = 7.28-7.24 (m, 2H), 7.18-7.14 (m, 3H), 3.45-3.38 (m, 2H), 2.09-1.94 (m, 2H), 1.75 (s, 3H), 1.59 (s, 3H), 1.43-1.35 (m, 2H), 1.20-1.11 (m, 1H), 0.90 (t, J = 7.4 Hz, 3H), 0.85 (d, J = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): (E isomer) δ = 140.7, 130.3, 129.1, 128.0, 127.9, 125.2, 41.7, 40.4, 33.8, 29.7, 19.0, 18.9, 18.5, 11.7; ¹H NMR (400 MHz, CDCl₃): (Z isomer) δ = 7.27-7.23 (m, 2H), 7.19-7.12 (m, 3H), 3.45-3.38 (m, 2H), 2.15-1.94 (m, 2H), 1.70 (s, 3H), 1.57 (s, 3H), 1.44-1.35 (m, 2H), 1.18-1.08 (m, 1H), 0.90 (t, J = 7.4 Hz, 3H), 0.85 (d, J = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): (Z isomer) δ = 140.6, 129.0, 128.2, 127.8, 127.0, 125.3, 41.7, 39.8, 33.8, 29.6, 19.1, 18.8, 18.4, 11.7; MS (EI) m/z (relative intensity, %) 216 (M⁺, 65), 159 (67), 145 (71), 131 (35), 117 (100), 105 (11), 91(43), 83 (8), 69 (21), 55 (8), 41 (14), 29 (7); HR-MS: calcd for C₁₆H₂₄: 216.1878, found: 216.1883; elemental analysis: calcd for C₁₆H₂₄: C, 88.82; H, 11.18. found: C, 88.65; H, 11.37.
1-Cyclohexyl-2,3-dimethyl-4-phenyl-2-butene (4g).

To a THF solution (3.8 mL) of cyclohexyl iodide (242 mg, 1.2 mmol), 2,3-dimethyl-1,3-butadiene (120 mg, 1.0 mmol), and a catalytic amount of [(dppf)NiCl₂] (53 mg, 0.08 mmol) was added a hexane solution of PhZnCl (0.4 M, 3.8 mL, 1.5 mmol) and at 0 °C under nitrogen. After stirring for 24 h at 25 °C, 1 N HCl aq was added to the solution. Similar workup as mentioned above afforded a pale yellow crude product (78% NMR yield). Purification by HPLC with CHCl₃ as an eluent afforded 175 mg (72%) of 4g. ¹H NMR showed a mixture of stereoisomers with an E/Z ratio of 67/33. IR (neat): 3061, 3025, 2923, 2850, 1602, 1493, 1449, 1373, 842, 762 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): (E isomer) δ = 7.23-7.18 (m, 2H), 7.12-7.06 (m, 3H), 3.33 (s, 2H), 1.93 (d, J = 7.3 Hz, 2H), 1.68 (s, 3H), 1.64-1.49 (m, 4H), 1.51 (s, 3H), 1.42-1.36 (m, 1H), 1.19-1.02 (m, 4H), 0.88-0.80 (m, 2H); NOE difference measurement: irradiation of methylene protons at δ 3.33 (-CH₂-C₆H₅) caused enhancement of the two methyl protons at δ 1.68 (8%) and 1.51 (4%) respectively while no enhancement was observed for methylene protons at δ 1.93 (-CH₂-cyclohexyl). ¹³C NMR (100 MHz, CDCl₃): (E isomer) δ = 140.9, 128.9, 128.3, 128.1, 127.6, 125.5, 42.5, 40.5, 37.2, 33.6, 26.8, 26.7, 19.3, 18.7; ¹H NMR (400 MHz, CDCl₃): (Z isomer) δ = 7.21-7.17 (m, 2H), 7.11-7.06 (m, 3H), 3.34 (s, 2H), 1.99 (d, J = 7.1 Hz, 2H), 1.78-1.51 (m, 4H), 1.63 (s, 3H), 1.49 (s, 3H), 1.41-1.31 (m, 1H), 1.18-1.00 (m, 4H), 0.86-0.78 (m, 2H); NOE difference measurement: irradiation of methylene protons at δ 1.99 (-CH₂-C₆H₅) caused enhancement of the one methylene proton at δ?1.93 (9%) and one methyl proton at δ 1.49 (5%) respectively. ¹³C NMR (100 MHz, CDCl₃): (Z isomer) δ = 141.0, 128.9, 128.4, 128.0, 127.1, 125.5, 42.4, 40.0, 37.2, 33.6, 26.8, 26.7, 19.2, 18.6. MS (EI) m/z (relative intensity, %) 242 (M⁺, 80), 159 (45), 146 (66), 145 (100), 131 (35), 117 (71), 91 (41), 81(12), 69 (12), 55 (27), 41 (19); HR-MS: calcd for C₁₈H₂₆: 242.2034, found: 242.2016; elemental analysis: calcd for C₁₈H₂₆: C, 89.19; H, 10.81. found: C, 88.93; H, 10.63.
4-(2,3,5,5-Tetramethylhex-2-enyl)benzoic acid ethyl ester (4h).

To a mixture of t-butyl bromide (163 mg, 1.2 mmol), 2,3-dimethyl-1,3-butadiene (85 mg, 1.0 mmol), and a catalytic amount of [(dppf)NiCl$_2$] (58 mg, 0.08 mmol) was added a THF solution of p-EtO$_2$C$_6$H$_4$ZnI (0.5 M, 3.0 mL, 1.5 mmol) at 0 °C under nitrogen. After stirring for 24 h at 25 °C, 1 N HCl aq was added to the solution. Similar workup as mentioned above afforded a pale yellow crude product (75% NMR yield). Purification by HPLC with CHCl$_3$ as an eluent afforded 205 mg (69 %) of 4h. IR (neat): 2953, 2866, 1716, 1414, 1365, 1275, 1175, 1106, 1122, 746 cm$^{-1}$, $^1$H NMR (400 MHz, CDCl$_3$): (E isomer) $\delta$ = 7.96-7.22 (m, 2H), 7.20-7.16 (m, 2H), 4.36 (q, $J$ = 7.0 Hz, 2H), 3.47 (s, 2H), 2.10 (s, 2H), 1.77 (s, 3H), 1.53 (s, 3H), 1.38 (t, $J$ = 7.0 Hz, 3H), 0.95 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$): (E isomer) $\delta$ = 166.5, 146.5, 129.4, 129.1, 128.4, 128.3, 128.0, 60.6, 47.9, 40.7, 33.2, 30.5, 21.9, 18.5, 14.3; $^1$H NMR (400 MHz, CDCl$_3$): (Z isomer) $\delta$ = 7.97-7.93 (m, 2H), 7.26-7.22 (m, 2H), 4.36 (q, $J$ = 7.0 Hz, 2H), 3.47 (s, 2H), 2.17 (s, 2H), 1.81 (s, 3H), 1.58 (s, 3H), 1.38 (t, $J$ = 7.0 Hz, 3H), 0.95 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$): (Z isomer) $\delta$ = 166.5, 146.4, 129.5, 129.3, 128.3, 128.2, 128.0, 60.6, 48.0, 40.7, 33.6, 30.6, 22.0, 19.7, 14.3. MS (EI) m/z (relative intensity, %) 288 (M$^+$, 23), 243 (23), 232 (100), 217 (24), 203 (36), 189 (12), 173 (7), 159 (54), 145 (19), 128 (10), 117 (19), 91 (6), 57 (48), 41 (11), 29 (13); HR-MS: calcd for C$_{19}$H$_{28}$O$_2$: 288.2090, found: 288.2097. elemental analysis: calcd for C$_{19}$H$_{28}$O$_2$: C, 79.12; H, 9.78. found: C, 79.31; H, 10.00.