Nickel-Catalyzed Highly Regio- and Stereoselective Three-Component Assembly of Allenes, Aryl Iodides and Alkenylzirconium Reagents

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Experimental Section

Synthesis of Alkenylzirconium Reagent: A terminal alkyne ($\text{RC}\equiv\text{CH}$, 2.00 mmol) was added to a suspension of Cp_2ZrHCl (1.25 mmol) in THF (2.0 mL) at room temperature. The resulting mixture was stirred at room temperature for 2 h. During the reaction, light yellow color of the solution was developed. The solution was evacuated to remove the excess alkyne and solvent. Then freshly distilled THF (2.0 mL) was added and this resulting mixture ($\text{ZrCp}_2\text{ClCH=CHR}^2$) was used for the subsequent nickel-catalyzed reaction. This procedure of generating alkenylzirconium reagent ($\text{ZrCp}_2\text{ClCH=CHR}^2$) was used for all alkynes except phenyl acetylene ($\text{R}^2 = \text{Ph}$). The alkenylzirconium reagent from phenyl acetylene was generated using 1.5 mmol of the alkyne and no further evacuation or addition of THF was done.

General Procedure for Nickel-Catalyzed Three-Component Reaction: A round-bottom side-arm flask (25 mL) containing $\text{NiCl}_2(\text{PPh}_3)_2$ (0.025 mmol, 5.0 mol%) and zinc powder (2.75 equiv) was evacuated and purged with nitrogen gas three times. To the system, freshly distilled THF (1.0 mL), an aryl iodide (0.50 mmol), allene (1.00 mmol), and alkenylzirconium reagent (1.25 mmol in 2 mL THF) were added sequentially and the reaction mixture was stirred at 50 °C for 24 h. The reaction mixture was cooled to room temperature, diluted with a mixture of ethyl acetate and hexane (20:80) and then stirred in the air for 15 min. The mixture was filtered through a short Celite and silica-gel pad and washed with a mixture of ethyl acetate and hexane solution several times. The filtrate was concentrated and the residue was purified on a silica-gel column using hexane-ethyl acetate as eluent to afford the three-component assembly product **4**. Compounds **4a-q** were synthesized according to this procedure and the spectral data of these compounds are as follows.

(1E,4E)-1-Cyclohexyl-2-(4-methoxyphenyl)-1,4-octadiene (4a): oil; ^1H NMR (400 MHz, CDCl_3): δ = 0.80 (3H, t, J = 7.6 Hz), 1.10-1.32 (7H, m), 1.66-1.73 (5H, m),

1.89-1.91 (2H, m), 2.26-2.37 (1H, m), 3.14 (2H, d, $J = 4.8$ Hz), 3.77 (3H, s), 5.37-5.42 (2H, m), 5.52 (1H, d, $J = 9.2$ Hz), 6.80 (2H, d, $J = 8.8$ Hz), 7.29 (2H, d, $J = 8.8$ Hz); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): $\delta = 13.5, 22.6, 26.0, 26.1, 31.8, 33.3, 34.6, 37.6, 55.3, 113.4, 127.2, 128.3, 131.0, 134.3, 135.0, 135.8, 158.3$; HRMS (m/z): calcd for $\text{C}_{21}\text{H}_{30}\text{O}$ 298.2297, found 298.2294.

1-(4- $\{(E)\text{-}1\text{-}[(E)\text{-}1\text{-Cyclohexylmethylidene]-3\text{-heptenyl}\}$ phenyl)-1-ethanone

(4b): oil; ^1H NMR (400 MHz, CDCl_3): $\delta = 0.80$ (3H, t, $J = 7.2$ Hz), 1.13-1.33 (7H, m), 1.58-1.72 (5H, m), 1.89-1.91 (2H, m), 2.31-2.41 (1H, m), 2.56 (3H, s), 3.18 (2H, d, $J = 4.4$ Hz), 5.38-5.42 (2H, m), 5.73 (1H, d, $J = 9.6$ Hz), 7.43 (2H, d, $J = 8.0$ Hz), 7.85 (2H, d, $J = 8.0$ Hz); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): $\delta = 13.5, 22.5, 25.8, 26.0, 26.5, 29.7, 33.1, 34.6, 37.8, 126.2, 127.7, 128.3, 131.6, 135.0, 135.1, 137.9, 148.1, 197.7$; HRMS (m/z): calcd for $\text{C}_{22}\text{H}_{30}\text{O}$ 310.2297, found 310.2308.

(1E,4E)-1-Cyclohexyl-2-(4-methylphenyl)-1,4-octadiene (4c): oil; ^1H NMR (500 MHz, CDCl_3): $\delta = 0.82$ (3H, t, $J = 7.5$ Hz), 1.08-1.41 (8H, m), 1.65-1.79 (5H, m), 1.91-1.96 (2H, m), 2.30 (3H, s), 3.14 (2H, d, $J = 4.0$ Hz), 5.38-5.42 (2H, m), 5.56 (1H, d, $J = 9.5$ Hz), 7.06 (2H, d, $J = 8.0$ Hz), 7.25 (2H, d, $J = 8.0$ Hz); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): $\delta = 13.5, 21.0, 22.6, 26.0, 26.1, 33.3, 33.4, 34.6, 37.6, 126.0, 128.3, 128.7, 131.0, 135.0, 135.4, 135.9, 140.4$; HRMS (m/z): calcd for $\text{C}_{21}\text{H}_{30}$ 282.2348, found 282.2341.

2- $\{(E)\text{-}1\text{-}[(E)\text{-}1\text{-Cyclohexylmethylidene]-3\text{-heptenyl}\}$ thiophene (4d): oil; ^1H NMR (500 MHz, CDCl_3): $\delta = 0.82$ (3H, t, $J = 7.5$ Hz), 1.09-1.36 (7H, m), 1.65-1.73 (5H, m), 1.92-1.98 (2H, m), 2.27-2.38 (1H, m), 3.14 (2H, d, $J = 5.5$ Hz), 5.40-5.51 (2H, m), 5.76 (1H, d, $J = 10.0$ Hz), 6.90 (1H, t, $J = 4.0$ Hz), 6.94 (1H, d, $J = 4.0$ Hz), 7.04 (1H, d, $J = 4.0$ Hz); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): $\delta = 13.6, 22.6, 25.9, 26.0,$

33.1, 33.7, 34.6, 37.5, 122.4, 122.7, 127.1, 127.7, 129.9, 131.5, 134.4, 147.3; HRMS (m/z): calcd for C₁₈H₂₆S 274.1755, found 274.1768.

(1E,4E)-1-Cyclohexyl-2-(2-methoxyphenyl)-1,4-octadiene (4e): oil; ¹H NMR (500 MHz, CDCl₃): δ = 0.80 (3H, t, *J* = 8.0 Hz), 1.06-1.35 (7H, m), 1.55-1.72 (5H, m), 1.80-1.85 (2H, m), 2.34-2.41 (1H, m), 3.13 (2H, d, *J* = 6.0 Hz), 3.76 (3H, s) 5.20-5.38 (3H, m), 6.80 (1H, d, *J* = 8.0 Hz), 6.85 (1H, dd, *J*₁ = 1.0 Hz, *J*₂ = 6.0 Hz), 7.04 (1H, d, *J* = 8.0 Hz), 7.18 (1H, dd, *J*₁ = 1.0 Hz, *J*₂ = 6.0 Hz); ¹³C{¹H} NMR (125 MHz, CDCl₃): δ = 13.5, 22.7, 26.0, 26.1, 33.3, 34.0, 34.6, 37.1, 55.4, 111.6, 120.3, 127.7, 128.5, 130.5, 130.9, 133.7, 136.2, 136.8, 156.7; HRMS (m/z): calcd for C₂₁H₃₀O 298.2297, found 298.2289.

(1E,4E)-1-Cyclohexyl-2-(3-methoxyphenyl)-1,4-octadiene (4f): oil; ¹H NMR (500 MHz, CDCl₃): δ = 0.80 (3H, t, *J* = 7.5 Hz), 1.08-1.32 (7H, m), 1.66-1.89 (5H, m), 1.88-1.93 (2H, m), 2.24-2.37 (1H, m), 3.14 (2H, d, *J* = 5.0 Hz), 3.78 (3H, s) 5.38-5.43 (2H, m), 5.61 (1H, d, *J* = 9.5 Hz), 6.78 (1H, d, *J* = 8.0 Hz), 6.91 (1H, s), 6.95 (1H, d, *J* = 8.0 Hz), 7.17 (1H, t, *J* = 8.0 Hz); ¹³C{¹H} NMR (125 MHz, CDCl₃): δ = 13.5, 22.6, 25.9, 26.0, 33.2, 33.5, 34.6, 37.7, 55.2, 111.6, 112.1, 118.8, 128.2, 128.5, 128.6, 131.1, 135.9, 145.0, 159.4; HRMS (m/z): calcd for C₂₁H₃₀O 298.2297, found 298.2300.

Ethyl 4-[(E)-1-[(E)-1-cyclohexylmethylidene]-3-heptenyl]benzoate (4g): oil; ¹H NMR (400 MHz, CDCl₃): δ = 0.79 (3H, t, *J* = 7.2 Hz), 1.10-1.35 (7H, m), 1.38 (3H, t, *J* = 7.2 Hz), 1.56-1.81 (5H, m), 1.87-1.92 (2H, m), 2.27-2.38 (1H, m), 3.17 (2H, d, *J* = 4.8 Hz), 4.34 (2H, q, *J* = 7.2 Hz), 5.37-5.43 (2H, m), 5.70 (1H, d, *J* = 9.6 Hz), 7.41 (2H, d, *J* = 8.4 Hz), 7.92 (2H, d, *J* = 8.4 Hz); ¹³C{¹H} NMR (125 MHz, CDCl₃): δ = 13.5, 14.4, 22.5, 25.9, 26.0, 29.7, 33.1, 34.6, 37.8, 60.8, 126.0, 127.7, 128.3, 129.4, 131.5, 135.1, 137.6, 147.8, 166.7; HRMS (m/z): calcd for C₂₃H₃₂O₂ 340.2402, found 340.2409.

(1E,4E)-2-(4-Methoxyphenyl)-1-phenyl-1,4-octadiene (4h): oil; ^1H NMR (500 MHz, CDCl_3): δ = 0.81 (3H, t, J = 8.0 Hz), 1.28-1.38 (2H, m), 1.92-1.97 (2H, m), 3.36 (2H, d, J = 4.0 Hz), 3.81 (3H, s) 5.42-5.51 (2H, m), 6.80 (1H, s), 6.87 (2H, d, J = 8.5 Hz), 7.21-7.37 (5H, m), 7.45 (2H, d, J = 8.5 Hz); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ = 13.5, 22.5, 33.5, 34.7, 55.3, 113.6, 126.5, 127.3, 127.5, 127.6, 128.2, 128.7, 132.2, 135.1, 138.2, 139.4, 158.9; HRMS (m/z): calcd for $\text{C}_{21}\text{H}_{24}\text{O}$ 292.1827, found 292.1825.

1-(4-{(E)-1-[(E)-1-Cyclohexylmethylidene]-4-phenyl-3-butenyl}phenyl)-1-ethanone (4i): oil; ^1H NMR (500 MHz, CDCl_3): δ = 1.15-1.39 (5H, m), 1.65-1.75 (4H, m), 2.37-2.42 (2H, m), 2.56 (3H, s), 3.41 (2H, d, J = 5.0 Hz), 5.83 (1H, d, J = 10.0 Hz), 6.19 (1H, dt, J_1 = 1.0 Hz, J_2 = 16.0 Hz), 6.38 (1H, d, J = 16.0 Hz), 7.16-7.27 (5H, m), 7.47 (2H, d, J = 8.0 Hz), 7.86 (2H, d, J = 8.0 Hz); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ = 25.9, 26.6, 29.7, 33.1, 33.3, 38.0, 126.0, 126.2, 127.1, 128.2, 128.4, 128.5, 130.7, 134.1, 135.2, 137.4, 138.7, 147.7, 197.8; HRMS (m/z): calcd for $\text{C}_{25}\text{H}_{28}\text{O}$ 344.2140, found 344.2147.

1-Methoxy-4-{(E)-4-phenyl-1-[(E)-1-phenylmethylidene]-3-butenyl}benzene (4j): oil; ^1H NMR (400 MHz, CDCl_3): δ = 3.58 (2H, d, J = 5.2 Hz), 3.79 (3H, s), 6.33 (1H, dt, J_1 = 4.0 Hz, J_2 = 16.0 Hz), 6.44 (1H, d, J = 16.0 Hz), 6.88 (1H, s), 6.90 (2H, d, J = 8.0 Hz), 7.07-7.39 (10H, m), 7.49 (2H, d, J = 8.0 Hz); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ = 33.8, 55.3, 113.8, 126.1, 126.7, 127.0, 127.5, 128.0, 128.2, 128.3, 128.4, 128.7, 131.2, 134.8, 137.5, 138.0, 138.5, 159.0; HRMS (m/z): calcd for $\text{C}_{24}\text{H}_{22}\text{O}$ 326.1671, found 326.1669.

(1E,4E)-1-Cyclohexyl-2-(4-methoxyphenyl)-6,6-dimethyl-1,4-heptadiene (4k): oil; ^1H NMR (500 MHz, CDCl_3): δ = 0.92 (9H, s), 1.05-1.38 (7H, m), 1.65-1.73 (3H, m), 2.26-2.29 (1H, m), 3.11 (2H, d, J = 5.5 Hz) 3.78 (3H, s), 5.29 (1H, dt, J_1 = 6.0 Hz,

$J_2 = 16.0$ Hz), 5.47 (1H, d, $J = 16.0$ Hz), 5.51 (1H, d, $J = 9.5$ Hz), 6.79 (2H, d, $J = 8.5$ Hz), 7.27 (2H, d, $J = 8.5$ Hz); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): $\delta = 26.0, 26.1, 29.6, 29.7, 33.3, 33.7, 37.7, 55.3, 113.4, 122.7, 127.2, 134.5, 135.0, 136.1, 142.1, 158.2$; HRMS (m/z): calcd for $\text{C}_{22}\text{H}_{32}\text{O}$ 312.2453, found 312.2452.

1-{4-[(*E*)-1-[(*E*)-1-Cyclohexylmethylidene]-4-(1,1,1-trimethylsilyl)-3-butenyl]phenyl}-1-ethanone (4l): oil; ^1H NMR (500 MHz, CDCl_3): $\delta = 0.00$ (9H, s), 1.07-1.37 (7H, m), 1.46-1.79 (3H, m), 2.23-2.32 (1H, m), 2.58 (3H, s), 3.28 (2H, d, $J = 6.0$ Hz), 5.70 (1H, d, $J = 16.0$ Hz), 5.78 (1H, d, $J = 9.5$ Hz), 6.03 (1H, dt, $J_1 = 5.0$ Hz, $J_2 = 16.0$ Hz), 7.41 (2H, d, $J = 8.5$ Hz), 7.86 (2H, d, $J = 8.5$ Hz); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): $\delta = -1.1, 25.8, 26.0, 26.4, 32.9, 37.2, 38.0, 126.1, 128.1, 130.9, 133.8, 135.1, 138.8, 143.7, 148.2, 197.8$; HRMS (m/z): calcd for $\text{C}_{22}\text{H}_{32}\text{OSi}$ 340.2222, found 340.2224.

1-(4-{(*E*)-1-[(*E*)-1-Cycloheptylmethylidene]-3-heptenyl}phenyl)-1-ethanone (4p): oil; ^1H NMR (400 MHz, CDCl_3): $\delta = 0.79$ (3H, t, $J = 7.6$ Hz), 1.21-1.79 (15H, m), 1.88-1.92 (2H, m), 2.56 (3H, s), 3.17 (2H, d, $J = 4.4$ Hz), 5.38-5.42 (2H, m), 5.82 (1H, d, $J = 9.6$ Hz), 7.43 (2H, d, $J = 8.4$ Hz), 7.85 (2H, d, $J = 8.4$ Hz); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): $\delta = 13.8, 22.9, 26.8, 28.8, 33.3, 34.9, 35.2, 39.6, 126.6, 127.9, 128.6, 131.9, 133.9, 135.4, 139.1, 148.6, 198.1$; HRMS (m/z): calcd for $\text{C}_{23}\text{H}_{32}\text{O}$ 324.2453, found 324.2447.

Ethyl (2*Z*,6*E*)-4-[(*E*)-1-cyclohexylmethylidene]-7-phenyl-2,6-heptadienoate (4q): oil; ^1H NMR (400 MHz, CDCl_3): $\delta = 1.03$ -1.23 (7H, m), 1.27 (3H, t, $J = 6.8$ Hz), 1.63-1.78 (3H, m), 2.35-2.41 (1H, m), 3.15 (2H, d, $J = 6.0$ Hz), 4.17 (2H, q, $J = 6.8$ Hz), 5.82 (1H, d, $J = 6.4$ Hz), 5.86 (1H, d, $J = 8.0$ Hz), 6.16 (1H, dt, $J_1 = 6.0$ Hz, $J_2 = 16.0$ Hz), 6.34 (1H, d, $J = 16.0$ Hz), 7.19 (1H, d, $J = 8.4$ Hz), 7.25-7.38 (5H, m); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): $\delta = 14.6, 25.9, 26.1, 30.4, 32.8, 38.2, 60.5, 116.5,$

126.3, 127.4, 127.6, 128.8, 130.9, 133.1, 137.7, 148.9, 149.4, 167.8; HRMS (m/z): calcd for C₂₂H₂₈O₂ 324.2089, found 324.2086.

NOE experimental data of compound 4a: Selective irradiation of methylene protons H_a at δ 3.14 led to the enhancement of the signals of cyclohexyl proton H_b at δ 2.30 by 2.34%, aromatic protons H_d at δ 7.29 by 1.43% and olefin proton H_e at 5.40 by 1.35%, whereas irradiation of the olefin proton H_c at δ 5.52 caused the enhancement of the signal of aromatic protons H_d at δ 7.29 by 1.79%. These NOE results strongly support the proposed (*E*) structure of product **4a** shown below.

The NOE results of compounds **4a**, **4b**, **4d** and **4q** are also listed below.

NOE experimental data of compound **4a**

NOE experimental data of compound **4b**

NOE experimental data of compound **4d**

NOE experimental data of compound **4q**