Supporting Information for
A New Zirconium-Mediated Approach Towards Regio- and Stereocontrolled
Synthesis of *trans*-Enediynes

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Experimental section

All reactions were carried out using standard Schlenk techniques under nitrogen. THF was distilled from sodium and benzophenone. Zirconocene dichloride and Ethylmagnesium bromide (1.0 M solution in THF) were purchased from Aldrich Chemical Company. Starting material such as alkynes and 1,4-bis(trimethylsilyl)-1,3-butadiyne were purchased from Acros Co. Ltd. Alkynyl bromides were prepared according to the published methods.

^1H and ^{13}C NMR spectra were recorded at room temperature in CDCl_3 (containing 1% TMS) solutions on Varian XL-300 MHz spectrometer. GC analysis was performed on SHIMADZU GC-14B equipped with fused silica capillary column SHIMADZU CBP1-M25-O25 and SHIMADZU CR8A-Chromatopac integrator. High-resolution mass spectra was obtained by using IonSpec 4.7 Tesla FTMS, Concept 1H Series and APEXIII 7.0 Tesla FTMS mass spectrometers. Single crystal X-ray diffraction data were collected on Bruker SMART APEX diffractometers with molybdenum cathodes.

A typical procedure for the formation of *trans*-enediynes.

To a solution of Cp_2ZrCl_2 (0.365 g, 1.25 mmol) in THF (5 ml) was added EtMgBr (1.0 M THF solution, 2.5 mmol) at $-50\text{ }^\circ\text{C}$. After stirring for 1 h at the same temperature, 1,4-bis(trimethylsilyl)buta-1,3-diyne (0.19 g, 1 mmol) was added and the reaction mixture was warmed up to room temperature and stirred for 2 h. Allyloxytrimethylsilane (0.26g, 2 mmol) was added and the mixture was heated up to

50 °C for 3 h. Then, to the reaction solution was added 1 equiv of alkynyl bromide and 5 mol% of CuCl. The mixture was stirred at 50 °C for 1 h. After quenching the reaction mixture with 3N HCl, it was extracted with ether. Combined organic extracts were washed with aqueous NaHCO₃ and water, dried over Na₂SO₄, and concentrated in a vacuum. Column chromatography on silica gel afforded the corresponding products. A light-yellow oil of allylated enyne derivative **2a** (237 mg, 62%) was obtained. GC yield: 98%.

1-Nitro-4-(Z-3-Trimethylsilyl-4-trimethylsilylethynylhepta-3,6-dien-1-ynyl)benzene (2a). GC yield 98%. Column chromatography on silica gel (petroleum ether/ethyl acetate =50:1) afforded 237 mg (62%) product as a light yellow liquid. ¹H NMR (CDCl₃, Me₄Si) δ 0.20 (s, 9H), 0.34 (s, 9H), 3.30 (d, *J*=6.9Hz, 2H), 5.05-5.16 (m, 2H), 5.84-5.90 (m, 1H), 7.47-7.53 (m, 2H), 8.12-8.16 (m, 2H); ¹³C NMR (CDCl₃, Me₄Si) δ -1.20, -0.04, 42.18, 95.75, 105.82, 106.00, 116.60, 123.53, 123.60, 130.76, 130.95, 131.73, 134.14, 142.77. HRMS(EI) calcd for C₂₁H₂₇NO₂Si₂ 381.1580, found 381.1585.

1-Methyl-4-(Z-3-trimethylsilyl-4-trimethylsilylethynylhepta-3,6-dien-1-ynyl)benzene (2b). GC yield 90%. Column chromatography on silica gel (petroleum ether) afforded 266 mg (76%) product as a light yellow liquid. ¹H NMR (CDCl₃, Me₄Si) δ 0.22 (s, 9H), 0.35 (s, 9H), 2.35 (s, 3H), 3.33-3.36 (m, 2H), 5.06-5.20 (m, 2H), 5.90-5.96 (m, 1H), 7.10-7.13 (m, 2H), 7.31-7.32 (m, 2H); ¹³C NMR (CDCl₃, Me₄Si) δ -1.09, -0.34, 21.49, 41.93, 89.84, 103.78, 104.34, 106.64, 116.23, 121.06, 129.08,

131.14, 132.12, 134.68, 138.18, 139.69. HRMS(EI) calcd for $C_{22}H_{30}Si_2$ 350.1886, found 350.1873.

1-Chloro-4-(Z-3-trimethylsilyl-4-trimethylsilylethynylhepta-3,6-dien-1-ynyl)benzene (2c). GC yield 85%. Column chromatography on silica gel (petroleum ether) afforded 248 mg (67%) product as a light yellow liquid. 1H NMR ($CDCl_3$, Me_4Si) δ 0.19 (s, 9H), 0.31 (s, 9H), 3.30 (d, $J=6.6Hz$, 2H), 5.04-5.17 (m, 2H), 5.89-5.92 (m, 1H), 7.23-7.33 (m, 4H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ -1.12, -0.37, 42.01, 91.36, 102.68, 104.48, 106.38, 116.37, 122.60, 128.66, 131.55, 132.40, 134.00, 134.50, 140.72. HRMS(EI) calcd for $C_{21}H_{27}ClSi_2$ 370.1340, found 370.1341.

1-Methoxy-4-(Z-3-trimethylsilyl-4-trimethylsilylethynylhepta-3,6-dien-1-ynyl)benzene (2d). GC yield 73%. Column chromatography on silica gel petroleum ether/ethyl acetate =100:1) afforded 220 mg (60%) product as a light yellow liquid. 1H NMR ($CDCl_3$, Me_4Si) δ 0.25 (s, 9H), 0.38 (s, 9H), 3.38 (d, $J=6.9Hz$, 2H), 3.81 (s, 1H), 5.10-5.23 (m, 2H), 5.96-5.99 (m, 1H), 6.86 (d, $J=6.9Hz$, 2H), 7.38 (d, $J=8.9Hz$, 2H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ -1.09, -0.3, 41.87, 55.14, 89.28, 103.55, 104.36, 106.74, 113.95, 116.19, 116.27, 132.20, 132.67, 134.68, 139.07, 159.52. HRMS(EI) calcd for $C_{22}H_{30}OSi_2$ 366.1835, found 366.1848.

1,3-Dichloro-2-(Z-3-trimethylsilyl-4-trimethylsilylethynylhepta-3,6-dien-1-ynyl)benzene (2e). GC yield 76%. Column chromatography on silica gel petroleum ether)

afforded 295 mg (73%) product as a light yellow liquid. ^1H NMR (CDCl_3 , Me_4Si) δ 0.22 (s, 9H), 0.37 (s, 9H), 3.48 (d, $J=6.3\text{Hz}$, 2H), 5.06-5.12 (m, 2H), 5.95 (m, 1H), 7.10 (m, 1H), 7.30 (d, $J=8.1\text{Hz}$, 2H); ^{13}C NMR (CDCl_3 , Me_4Si) δ -0.82, -0.39, 42.24, 96.93, 100.83, 105.41, 106.31, 116.35, 124.00, 127.52, 128.63, 130.97, 134.57, 137.02, 142.89. HRMS(EI) calcd for $\text{C}_{21}\text{H}_{26}\text{Cl}_2\text{Si}_2$ 404.0950, found 404.0960.

(Z-3-Trimethylsilyl-4-trimethylsilylethynylhepta-3,6-dien-1-ynyl)benzene (2f).

GC yield 65%. Column chromatography on silica gel (petroleum ether) afforded 202 mg (60%) product as a light yellow liquid. ^1H NMR (CDCl_3 , Me_4Si) δ 0.21 (s, 9H), 0.35 (s, 9H), 3.35 (d, $J=6.6\text{Hz}$, 2H), 5.07-5.20 (m, 2H), 5.93-5.96 (m, 1H), 7.28-7.44 (m, 5H); ^{13}C NMR (CDCl_3 , Me_4Si) δ -1.11, -0.36, 41.96, 90.39, 103.99, 104.02, 106.50, 116.28, 124.07, 128.02, 128.29, 131.21, 131.89, 134.58, 140.17. HRMS(EI) calcd for $\text{C}_{21}\text{H}_{28}\text{Si}_2$ 336.1730, found 336.1720.

1-Trifluoromethyl-4-(Z-3-Trimethylsilyl-4-trimethylsilylethynylhepta-3,6-dien-1-ynyl)benzene (2g). GC yield 63%. Column chromatography on silica gel (petroleum ether/ethyl acetate =100:1) afforded 246 mg (61%) product as a light yellow liquid. ^1H NMR (CDCl_3 , Me_4Si) δ 0.23 (s, 9H), 0.36 (s, 9H), 3.36 (d, $J=6.9\text{Hz}$, 2H), 5.08-5.21 (m, 2H), 5.90 (m, 1H), 7.50 (q, $J=8.4\text{Hz}$, 4H); ^{13}C NMR (CDCl_3 , Me_4Si) δ -1.14, -0.42, 42.16, 92.74, 102.22, 105.02, 106.26, 116.51, 122.19, 125.26 (q, $J=14.3\text{Hz}$), 125.80, 127.92, 129.44, 129.86, 131.24, 131.38, 134.38, 141.78; ^{19}F NMR (CDCl_3) δ -63.177. HRMS(EI) calcd for $\text{C}_{22}\text{H}_{27}\text{F}_3\text{Si}_2$ 404.1603, found 404.1588.

[Z-3-(Trimethylsilyl)-4-(trimethylsilylethynyl)hepta-3,6-dien-1-ynyl]propionate

(2h). GC yield 93%. Column chromatography on silica gel petroleum ether /ethyl acetate =100:1) afforded 202 mg (61%) product as a light yellow liquid. ¹H NMR (CDCl₃, Me₄Si) δ 0.18 (s, 9H), 0.28 (s, 9H), 1.26 (t, *J*=7.2Hz, 3H), 3.2 (m, 2H), 4.42 (q, *J*=7.2Hz, 2H), 5.00 (m, 2H), 5.80 (m, 1H); ¹³C NMR (CDCl₃, Me₄Si) δ -1.17, -0.57, 14.06, 42.46, 61.74, 86.82, 93.78, 105.29, 107.15, 116.98, 128.34, 133.66, 146.72, 154.34. HRMS(EI) calcd for C₁₈H₂₈O₂Si₂ 332.1628, found 332.1622.

(Z)-5-Trimethylsilyl-4-trimethylsilylethynylundeca-1,4-dien-6-yne (2i). GC yield 75%. Column chromatography on silica gel (petroleum ether) afforded 221 mg (70%) product as a light yellow liquid. ¹H NMR (CDCl₃, Me₄Si) δ 0.16 (s, 9H), 0.26 (s, 9H), 0.90 (t, *J*=6.9Hz, 3H), 1.37-1.54 (m, 4H), 2.41 (t, *J*=6.9Hz, 2H), 3.20 (d, *J*=6.9Hz, 2H), 5.0-5.1 (m, 2H), 5.8 (m, 1H); ¹³C NMR (CDCl₃, Me₄Si) δ -1.09, -0.31, 13.60, 19.90, 22.02, 31.11, 41.60, 81.20, 102.55, 105.61, 106.66, 115.87, 133.12, 134.86, 138.94. HRMS(MALDI/DHB) for C₁₉H₃₃Si₂ [M+H]⁺: calcd 317.2121, found 317.2115.

1-(Z-3-Trimethylsilyl-4-trimethylsilylethynylhepta-3,6-dien-1-ynyl)cyclohexene

(2j). GC yield 89%. Column chromatography on silica gel (petroleum ether) afforded 242 mg (71%) product as a light yellow liquid. ¹H NMR (CDCl₃, Me₄Si) δ 0.17 (s, 9H), 0.25 (s, 9H), 1.55-1.65 (m, 4H), 2.09-2.14 (m, 4H), 3.21 (d, *J*=6.9Hz, 2H),

5.00-5.12 (m, 2H), 6.07-6.08 (m, 1H), 6.85-6.87 (m, 1H); ^{13}C NMR (CDCl_3 , Me_4Si) δ -1.14, -0.33, 21.53, 22.35, 25.85, 29.36, 41.73, 88.00, 103.29, 106.36, 106.78, 116.04, 121.67, 132.39, 134.62, 134.75, 138.78. HRMS(EI) calcd for $\text{C}_{21}\text{H}_{32}\text{Si}_2$ 340.2043, found 340.2029.

Desilylation-dimerization of (Z)-enediynes **2d using Hay coupling method.¹**

To a stirred solution of **2d** (0.05g, 0.14 mmol) in THF (5 mL), MeOH (5 mL) was added K_2CO_3 (0.025g, 0.18 mmol) and stirred for 0.5 h. The mixture was filtered and the filtrate was concentrated *in vacuo* to give a crude oil of the desilylated compound which was used for the next step without further purification. The crude desilylated product was added to a mixture of TMEDA (0.10 mL, 0.7 mmol) and CuCl (0.07g, 0.7 mmol) in CH_2Cl_2 . The reaction mixture was stirred at room temperature for 2 h and extracted with ether, washed with brine, dried over MgSO_4 and concentrated *in vacuo* to give a solid, which was chromatographed on silica gel to afford the title compound **3c** in 61% yield.

((3Z,9Z)-3,10-bis(trimethylsilyl)-4,9-diallyl-1,12-bis(4-methoxyphenyl)dodeca-3,9-dien-1,5,7,11-tetrayne (3c**)).** ^1H NMR (CDCl_3 , Me_4Si) δ 0.37 (s, 18H), 3.39 (d, $J=6.6\text{Hz}$, 4H), 3.82 (s, 6H), 5.11-5.24 (m, 4H), 5.90 (m, 2H), 6.87 (d, $J=8.4\text{Hz}$, 4H), 7.38 (d, $J=8.4\text{Hz}$, 4H); ^{13}C NMR (CDCl_3 , Me_4Si) δ -0.10, 41.45, 55.24, 82.73, 87.14, 89.62, 106.90, 114.01, 116.03, 116.67, 132.80, 134.31, 136.37, 137.42, 159.72. UV/Vis (CHCl_3) $\lambda_{\text{max}}(\epsilon)$ [nm]= 401 (10,200). HRMS (MALDI/DHB) for $\text{C}_{38}\text{H}_{42}\text{O}_2\text{Si}_2\text{Na}$ $[\text{M}+\text{Na}]^+$: calcd 609.2621, found 609.2593.

A typical procedure for one-pot synthesis of butadiynes 3.

To a stirred solution of **2f** (0.5 mmol) in pyridine (5 mL), MeOH (5 mL) was added Cu(OAc)₂ · H₂O (0.15g, 0.75 mmol), CuCl (0.01g, 0.1 mmol), AgNO₃ (0.017g, 0.1 mmol) and stirred for 20 h at 60 °C until the starting material disappeared. The reaction mixture was washed with 1N HCl, extracted with ether, washed with brine, dried over MgSO₄ and concentrated *in vacuo* to give a solid, which was chromatographed on silica gel to afford **3a** in 49% yield.

((3Z,9Z)-3,10-bis(trimethylsilyl)-4,9-diallyl-1,12-bisphenyl-dodeca-3,9-dien-1,5,7,11-tetrayne (3a). ¹H NMR (CDCl₃, Me₄Si) δ 0.35 (s, 18H), 3.38 (m, 4H), 5.10-5.22 (m, 4H), 5.89-5.94 (m, 2H), 7.23-7.44 (m, 10H); ¹³C NMR (CDCl₃, Me₄Si) δ -0.10, 41.55, 82.92, 87.05, 90.53, 106.55, 116.80, 123.85, 128.33, 128.37, 131.28, 134.18, 136.24, 138.54. UV/Vis (CHCl₃) λ_{max}(ε) [nm]= 388 (8,200). LRMS (EI) calcd for C₃₆H₄₈Si₂ 526, found 526. HRMS (EI) calcd for C₃₆H₃₈Si₂ 526.2512, found 526.2510.

((3Z,9Z)-3,10-bis(trimethylsilyl)-4,9-diallyl-1,12-bis(4-chlorophenyl)dodeca-3,9-dien-1,5,7,11-tetrayne (3b). Isolation yield: 50%. ¹H NMR (CDCl₃, Me₄Si) δ 0.35 (s, 18H), 3.36 (d, *J*=6.6Hz, 4H), 5.11-5.22 (m, 4H), 5.90 (m, 2H), 7.28-7.36 (m, 8H); ¹³C NMR (CDCl₃, Me₄Si) δ -0.10, 41.58, 83.11, 87.06, 91.43, 105.24, 116.90, 122.31, 128.73, 132.45, 134.05, 134.34, 135.96, 138.98. UV/Vis (CHCl₃) λ_{max}(ε) [nm]= 390 (5,400). HRMS (MALDI/DHB) for C₃₆H₃₇Si₂Cl₂ [M⁺]: calcd 595.1811, found 595.1780.

A typical procedure for the coupling reaction of α -alkynylated zirconacyclopentene with allylic compounds or alkynes. To a solution of Cp_2ZrCl_2 (0.365 g, 1.25 mmol) in THF (5 ml) was added EtMgBr (1.0 M THF solution, 2.5 mmol) at $-50\text{ }^\circ\text{C}$. After stirring for 1h at the same temperature, 1,4-bis(trimethylsilyl)buta-1,3-diyne (0.19 g, 1 mmol) was added and the reaction mixture was warmed up to room temperature and stirred for 2 h. Allyloxytrimethylsilane (0.26g, 2 mmol) was added and the mixture was heated up to $50\text{ }^\circ\text{C}$ for 3 h. The reaction mixture was quenched with 3N HCl and extract with ethyl acetate. The extract was washed with water, brine and dried over Na_2SO_4 . The solvent was evaporated *in vacuo* and the residue was purified by chromatography on silica gel (petroleum ether, $60\text{-}90\text{ }^\circ\text{C}$). A light-yellow oil of allylated enyne derivative **5** (147 mg, 62%) was obtained. GC yield: 84%. **(Z)-6-trimethylsilyl-4-trimethylsilylmethylene-hex-1-en-5-yne (5).** ^1H NMR (CDCl_3 , Me_4Si) δ 0.14 (s, 9H), 0.17 (s, 9H), 2.90 (dd, $J=1.2, 7.2\text{Hz}$, 2H), 5.09 (m, 2H), 5.90 (m, 2H); ^{13}C NMR (CDCl_3 , Me_4Si) δ -1.14, -0.26, 44.97, 97.38, 106.25, 116.64, 135.07, 137.06, 138.71. HRMS(EI) calcd for $\text{C}_{13}\text{H}_{24}\text{Si}_2$ 236.1417, found 236.1411.

(Z)-1,4-Bis-trimethylsilyl-hex-3-en-1-yne (8)². GC yield 78%. Column chromatography on silica gel (petroleum ether, $60\text{-}90^\circ\text{C}$) afforded 126 mg (56%) product as a light yellow liquid. ^1H NMR (CDCl_3 , Me_4Si) δ 0.04 (s, 9H), 0.09 (s, 9H), 0.85 (t, $J=7.2\text{Hz}$, 3H), 2.05 (dq, $J=1.5, 7.5\text{Hz}$, 2H), 5.82 (t, $J=1.5\text{Hz}$, 1H); ^{13}C NMR (CDCl_3 , Me_4Si) δ -0.18, -0.26, 14.00, 30.67, 97.46, 105.48, 117.83, 161.31.

(3Z,4E)-4-Propyl-1-trimethylsilyl-3-trimethylsilylmethylene-oct-4-en-1-yne (7a).

GC yield 77%. Column chromatography on silica gel (petroleum ether: 60-90°C) afforded 181 mg (59%) product as a light yellow liquid. ^1H NMR (CDCl_3 , Me_4Si) δ 0.19 (s, 9H), 0.20 (s, 9H), 0.92 (q, $J=7.6\text{Hz}$, 4H), 1.40 (m, 4H), 2.10 (q, $J=7.3\text{Hz}$, 2H), 2.23 (m, 2H), 6.04 (s, 1H), 6.20 (t, $J=7.2$, 1H); ^{13}C NMR (CDCl_3 , Me_4Si) δ -0.10, -0.30, 13.97, 14.37, 22.16, 22.77, 29.03, 30.80, 98.59, 104.72, 132.40, 134.47, 138.62, 138.75. HRMS(MALDI/DHB) for $\text{C}_{18}\text{H}_{34}\text{Si}_2\text{Na}$ $[\text{M}+\text{Na}]^+$: calcd 329.2097, found 329.2093.

(1E,3Z)-(2-phenyl-5-trimethylsilyl-3-trimethylsilylmethylene-pent-1-en-4-ynyl)benzene(7b).

GC yield 89%. Column chromatography on silica gel (petroleum ether, 60-90°C) afforded 299 mg (80%) product as a light yellow liquid. ^1H NMR (CDCl_3 , Me_4Si) δ 0.04 (s, 9H), 0.17 (s, 9H), 5.65 (s, 1H), 7.12-7.26 (m, 11H); ^{13}C NMR (CDCl_3 , Me_4Si) δ -1.12, -0.27, 100.55, 103.90, 126.96, 127.38, 127.86, 128.71, 129.67, 130.18, 131.18, 136.81, 137.89, 139.64, 141.56, 141.62. HRMS (MALDI/DHB) for $\text{C}_{24}\text{H}_{30}\text{Si}_2\text{Na}$ $[\text{M}+\text{Na}]^+$: calcd 397.1784, found 397.1791.

References:

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Figure 1, X-ray single-crystal structure of **3c**.

3a

3a

3b