A Novel, Highly Selective, and General Methodology for the Synthesis of 1,5-Diene-Containing Oligoisoprenoids of All Possible Geometrical Combinations Exemplified by an Iterative and Convergent Synthesis of Coenzyme Q_{10}

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Supplemental Data

General. All manipulations were conducted under a dry argon atmosphere, unless otherwise noted. THF and ether were distilled from sodium benzophenone ketyl, and the other solvents were dried and distilled under argon prior to use. $ZnBr_2$ was flame-dried under vaccum. Flash chromatographic separations were carried out on 230 - 400 mesh silica gel 60. Gas chromatography was performed on an HP 6890 Gas Chromatograph using HP-5 capillary column (30 m X 0.32 mm, 0.5 μm film) with appropriate hydrocarbons as internal standards. IR spectra were recorded on Perkin-Elmer 1800 or 2000 FT-IR. ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini-200 or Inova-300 spectrometers. LRMS and HRMS data were obtained on Hewlett Packard 5995 GC-MS and Kratos MS-50 mass spectrometers, respectively.

(*E*)-1,4-Diiodo-2-methylbut-1-ene (1a): This compound was prepared from (*E*)-4-Iodo-3-methyl-3-buten-1-ol[a(i)] by treatment with PPh_3, I_2, and imidazole in CH_2Cl_2[a(iii)] in 85% yield and >98% stereoisomeric puirity: ^1H NMR (200 MHz, $CDCl_3$, Me_4Si) δ 1.85 (s, 3 H), 2.76 (t, J = 7.5 Hz, 2 H), 3.23 (t, J = 7.5 Hz, 2 H), 6.06 (s, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$, Me_4Si) δ 2.45, 23.13, 43.15, 77.92, 145.75; MS (EI) *m/z* (%) 322 (81) [M^+ - H_2O]; IR (neat) 3064, 1616, 1425, 1279, 1235, 1121 cm^{-1}.

(*Z*)-1,4-Diiodo-2-methylbut-1-ene (1b): This compound was prepared from (*Z*)-4-Iodo-3-methyl-3-buten-1-ol[a(ii)] by treatment with PPh_3, I_2, and imidazole in CH_2Cl_2[a(iii)] in 84% yield and >98% stereoisomeric puirity: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.82 (s, 3 H), 2.8 (t, J = 7.6 Hz, 2 H), 3.21 (t, J = 7.3 Hz, 2 H), 6.06 (s, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 0.4, 23.05, 42.48, 77.06, 145.73.

(*E*)-8-Iodo-6-methyl-1-trimethylsilyl-5-octen-1-yne: To a solution of 4-iodo-1-trimethylsilyl-1-butyne (**3**) (7.6 g, 30 mmol) in Et_2O (30 mL) was added dropwise at -78 °C a 1.7 M solution of *t*-BuLi (18.8 mL, 32 mmol) in pentane via syringe. After stirring for 30 min at -78 °C, a solution of flame-dried $ZnBr_2$ (6.8 g, 30 mmol) in THF was transferred via cannula into the reaction mixture which was then warmed to 0 °C. A solution of **1a** (6.4 g, 20 mmol) and $Cl_2Pd(dppf)(CH_2Cl_2)$ (326 mg, 0.4 mmol) in THF (30 mL) were added and the reaction completed within 2 h at 23 °C. The reaction mixture was quenched with H_2O (50 mL) and extracted with Et_2O. The combined organic layers were dried over $MgSO_4$ and evaporated, the crude oil was purified by flash column chromatography (hexanes) to give the title compound: 0.58 g (91%); ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.14 (s, 9 H), 1.64 (m, 3 H), 2.15-2.35 (m, 4 H), 2.54 (t, J = 7.7 Hz, 2 H), 3.22 (t, J = 7.7 Hz, 2 H), 5.25 (t, J = 5.1 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.13 (3 C), 4.63, 15.47, 20.03, 27.28, 43.72, 84.48, 106.98, 125.52, 135.01; HRMS calcd. For $C_{12}H_{21}SiI$ 320.0457, found 320.0450; IR(neat) 2175, 1427, 1248, 842 cm^{-1}.

(5*E*, 9*E*)-12-Iodo-6,10-dimethyl-1-trimethylsilyl-5,9-dodecadien-1-yne: (*E*)-8-Iodo-6-methyl-1-trimethylsilyl-5-octen-1-yne (6.40 g, 20 mmol) was lithiated with *t*-BuLi (24.7 mL, 42 mmol), zincated with $ZnBr_2$, and cross coupled with **1a** (7.73 g, 24 mmol) according to the procedure described above. The crude product was purified by flash column chromatography (hexanes) to give the title compound: 7.01 g (90%); >98% *E*, *E*; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.14 (s, 9 H), 1.61 (s, 3 H), 1.63 (s, 3 H), 2.0-2.25 (m, 8 H), 2.51 (t, J = 7.6 Hz, 2 H), 3.20 (t, J = 7.6 Hz, 2 H), 5.15-5.25 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$, Me_4Si) δ 0.12 (3 C), 4.82, 15.29,

16.09, 20.28, 26.44, 27.28, 39.26, 43.74, 84.19, 107.29, 122.80, 127.11, 133.38, 136.05; HRMS calcd. For $C_{17}H_{29}SiI+1$ 389.1162, found 389.1146; IR(neat) 2175, 1447, 1249, 1043, 842 cm^{-1}.

(5*E*, 9*E*, 13*E*)-16-Iodo-6,10,14-trimethyl-1-trimethylsilyl-5,9,13-hexadecatrien-1-yne (6): (5*E*, 9*E*)-12-Iodo-6,10-dimethyl-1-trimethylsilyl-5,9-dodecadien-1-yne (2.50 g, 6.4 mmol) was lithiated with *t*-BuLi (7.6 mL, 12.9 mmol), zincated with $ZnBr_2$, and cross coupled with **1a** (2.28 g, 7.0 mmol) according to the procedure described above. The crude product was purified by flash column chromatography (hexanes) to give the title compound **6**: 2.31 g (79%); >98% *E*, *E*,*E*; ^1H NMR (300 MHz, $CDCl_3$, Me_4Si) δ 0.14 (s, 9 H), 1.55-1.75 (m, 9 H), 1.95-2.35 (m, 12 H), 2.52 (t, J = 7.6 Hz, 2 H), 3.20 (t, J = 7.6 Hz, 2 H), 5.05-5.3 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, Me_4Si) δ 0.12 (3 C), 4.90, 15.29, 15.96, 16.14, 20.31, 26.54 (2 C), 27.31, 39.30, 39.63, 43.80, 84.18, 107.37, 122.53, 124.36, 127.26, 133.33, 134.54, 136.45; HRMS calcd. For $C_{22}H_{37}SiI+1$ 457.1788, found 457.1797; IR(neat) 2175, 1447, 1249, 1043, 842 cm^{-1}.

(all-*E*)-6,10,14,18,22-Pentamethyl-1-trimethylsilyl-5,9,13,17,21-tricosapentaen-1-yne: Compound **6** (1.21 g, 2.65 mmol) was lithiated with *t*-BuLi (3.3 mL, 5.6 mmol), zincated with $ZnBr_2$, and cross coupled with (*E*)-1-iodo-2,6-methyl-1,5-heptadiene[b] (**4**) (0.8 g, 3.2 mmol) according to the procedure described above. The crude product was purified by flash column chromatography (hexanes) to give the title compound: 0.99 g (83%); >98% stereoisomeric purity; ^1H NMR (300 MHz, $CDCl_3$, Me_4Si) δ 0.14 (s, 9 H), 1.60 (bs, 12 H), 1.62 (s, 3 H), 1.68 (s, 3 H), 1.9-2.3 (m, 20 H), 5.05-5.2 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$, Me_4Si) δ 0.11 (3 C), 16.00 (3 C), 16.12, 17.63, 20.32, 25.66, 26.57, 26.64 (2 C), 26.75, 27.35, 39.71 (4 C), 84.17, 107.38, 122.55, 124.11 124.25 (2 C), 124.41, 131.07, 134.76, 134.79, 134.92, 136.49; HRMS calcd. For $C_{31}H_{52}Si+1$ 453.3617, found 453.311; IR(neat) 2176, 1669, 1448, 1249, 1043, 842, 760 cm^{-1}.

(all-*E*)-2,6,10,14,18-Pentamethyl-2,6,10,14,18-tricosapentaen-22-yne: KOH (0.28 g, 5.0 mmol) was dissolved in 95% MeOH in water (50 mL). To this 0.1 M solution was added (all-*E*)-6,10,14,18,22-pentamethyl-1-trimethylsilyl-5,9,13,17,21-tricosapentaen-1-yne (0.72 g, 1.59

mmol). The mixture was refluxed for 2 h. Water (30 mL) was added and the mixture was extracted with Et_2O. The combined organic layers were dried over $MgSO_4$ and evaporated. The crude product was purified by flash column chromatography (hexanes) to give the title compound: 0.49 g (81%); ^{1}H NMR (200 MHz, $CDCl_3$, Me_4Si) δ 1.60 (bs, 12 H), 1.62 (s, 3 H), 1.68 (s, 3 H), 1.9-2.3 (m, 21 H), 5.05-5.25 (m, 5 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 15.89, 15.98 (2 C), 16.09, 17.65, 18.90, 25.67, 26.50, 26.64 (2 C), 26.74, 27.16, 39.63, 39.71 (3 C), 68.09, 84.41, 122.43, 124.04, 124.23 (2 C), 124.39, 131.12, 134.82 (2 C), 134.96, 136.64; HRMS calcd. For $C_{28}H_{44}$+1 381.3521, found 381.3511; IR(neat) 3313, 2171, 1668, 1447, 1383, 1248, 1105, 841, 630 cm^{-1}.

(all-*E*)-1-Iodo-2,6,10,14,18,22-hexamethyl-1,5,9,3,17,21-tricosahexaene: In a flame dried round-bottomed flask were charged with Cl_2ZrCp_2 (83 mg, 0.3 mmol) and 1,2-dichloroethane (10 mL). Me_3Al (0.22 mL, 2.3 mmol) was added dropwise via syringe at 0 °C, followed by a solution of (all-*E*)-2,6,10,14,18-pentamethyl-2,6,10,14,18-tricosapentaen-22-yne (445 mg, 1.1 mmol) in 1,2-dichloroethane (5 mL). After stirring at 23 °C for 6 h, the reaction mixture was cooled to -78 °C with a dry ice-acetone bath and a solution of I_2 (346 mg, 1.4 mmol) in 5 mL of THF was added via cannula. The reaction mixture was stirred at 0 °C for 15 min and then was carefully quenched with 3 N HCl, extracted with Et_2O, washed with $NaHCO_3$, brine and water, dried over $MgSO_4$, and evaporated. The crude product was purified by flash column chromatography (hexanes) to give the title compound: 0.52 g (88%); >98% stereoisomeric purity; ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ 1.59 (bs, 15 H), 1.67 (s, 3 H), 1.83 (s, 3 H), 1.95-2.25 (m, 20 H), 5.0-5.15 (m, 5 H), 5.86 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, Me_4Si) δ 15.98 (4 C), 17.64, 23.89, 25.66, 26.25, 26.58, 26.62, 26.64, 26.73, 39.48, 39.65, 39.69 (3 C), 74.77, 122.91, 124.05, 124.22 (2 C), 124.39, 131.03, 134.72, 134.75, 134.91, 134.94, 147.57; HRMS calcd. For $C_{29}H_{47}I$: 522.2723, found 522.2710; IR(neat) 1667, 1447, 1381, 1269, 1142, 841cm^{-1}.

(all-*E*)-6,10,14,18,22,26,30,34,38-Nonamethyl-1-trimethylsilyl-5,9,13,17,21,25,29,33,37-nonacontanonaen-1-yne: Compound **6** (0.45 g, 1.0 mmol) was lithiated with *t*-BuLi (1.2 mL, 2.1 mmol), zincated with $ZnBr_2$, and cross coupled with (all-*E*)-1-iodo-2,6,10,14,18,22-hexamethyl-1,5,9,3,17,21-tricosahexaene (0.51 g, 1.0 mmol) according to the procedure described above for the synthesis of (*E*)-8-iodo-6-methyl-1-trimethylsilyl-5-octen-1-yne. The crude product was purified by flash column chromatography (hexanes) to give the title compound: 0.61 g (86%); >98% stereoisomeric purity; ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ 0.16 (s, 9 H), 1.61 (bs, 24 H), 1.64 (s, 3 H), 1.69 (s, 3 H), 1.95-2.25 (m, 36 H), 5.05-5.5 (m, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$, Me_4Si) δ 0.13 (3 C), 15.99 (7 C), 16.14, 17.65, 20.33, 25.68, 26.60, 26.68 (6 C), 26.76, 27.37, 39.74 (8 C), 84.19, 107.41, 122.55, 124.11 124.26 (6 C), 124.41, 131.12, 134.83 (6 C), 134.97, 136.54; LRMS (CI), m/e 724 (M+) (trace), 319 (29), 251 (44), 245 (44), 231 (26), 211 (37), 143 (42), 101 (99), 91 (45), 81 (49), 73 (100); IR(neat) 2174, 1451, 1377, 1249, 1079, 843, 760 cm^{-1}.

(all-*E*)-2,6,10,14,18,22,26,30,34-Nonamethyl-2,6,10,14,18,22,26,30,34-nonacontanonaen-38-yne: (all-*E*)-6,10,14,18,22,26,30,34,38-Nonamethyl-1-trimethylsilyl-5,9,13,17,21,25,29,33,37-nonacontanonaen-1-yne was desilylated according to the procedure described above for the synthesis of (all-*E*)-2,6,10,14,18-pentamethyl-2,6,10,14,18-tricosapentaen-22-yne. The crude product was purified by flash column chromatography (hexanes) to give the title compound: 0.31 g (84%); >98% stereoisomeric purity; ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ 1.6 (bs, 24 H), 1.67 (s, 3 H), 1.74 (s, 3 H), 1.9-2.25 (m, 37 H), 5.0-5.25 (m, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$, Me_4Si) δ 15.99 (8 C), 17.65, 18.91, 25.68, 26.69 (6 C), 26.77 (2 C), 27.20, 39.75 (8 C), 68.10, 84.43, 122.83, 124.13 124.28 (6 C), 124.43, 131.07, 134.81 (7 C), 136.62; LRMS (CI), m/e 652 (M+) (trace), 409 (0.02), 243 (0.14), 217 (0.33), 215 (0.21), 203 (1.0), 189 (1.6), 81 (76), 69(100); IR(neat) 3314, 2175, 1668, 1448, 1383, 1249, 842, cm^{-1}.

2-((all-*E*)-3,7,11,15,19,23,27,31,35,39-Decamethyl-2,6,10,14,18,22,26,30,34,38-tetracontadecaenyl)-5,6-dimethyox-3-methyl-1,4-benzoquinone (Coenzyme Q_{10} or Ubiquinone-10)[c](2): In a round-bottomed flask were charged with Cl_2ZrCp_2 (19.7 mg, 0.067 mmol) and 1,2-dichloroethane (1 mL). Me_3Al (0.039 mL, 0.4 mmol) was added via a micro syringe at 0 °C. A solution of (all-*E*)-6,10,14,18,22,26,30,34,38-nonamethyl-1-trimethylsilyl-5,9,13,17,21,25,29,33,37-nonacontanonaen-1-yne (176 mg, 0.27 mmol) in 1,2-dichloroethane (1 mL) was added dropwise. The reaction mixture was warmed to 23 °C with subsequent stirring for 1 h. The volatiles were removed at 55 °C/20 mmHg, and the residue was extracted with hexanes (3 mL × 2) and the supernatant was transferred into another dry flask under Ar atmosphere. The hexanes was removed and replaced with THF (1 mL). The solution was then transferred via cannula to a mixture of a Ni catalyst, *in situ* generated by treating 7.1 mg (0.01 mmol) of $Cl_2Ni(PPh_3)_2$ with *n*-BuLi (0.02 mmol) and PPh_3 (5.7 mg, 0.02 mmol), and 2-chloromethyl-5,6-dimethyl-3-methyl-1,4-benzoquenone[d] (**5**) (74.5 mg, 0.32 mmol) in THF. The reaction mixture was stirred at 23 °C for 1 h, extracted with Et_2O, washed with $NaHCO_3$ and brine, dried over $MgSO_4$, and evaporated. The crude solid was purified by flash chromatography (hexanes) to give coenzyme Q_{10} (**2**) as a yellow solid: 211 mg (90%); >98% stereoisomeric purity; ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ 1.58 (s, 3 H), 1.60 (bs, 27 H), 1.68 (s, 3 H), 1.74 (s, 3 H), 1.95-2.2 (m, 36 H), 3.18 (d, J = 6.8 Hz, 2 H),3.98 (s, 3 H), 3.99 (s, 3 H), 4.94 (t, J = 7.1 Hz, 1 H), 5.0-5.2 (m, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$, Me_4Si) δ 11.92, 16.00 (8 C), 16.32, 17.66, 25.29, 25.69, 26.51, 26.71 (8 C), 26.76, 39.72 (4 C), 39.74 (4 C), 61.11 (2 C), 118.85, 123.84, 124.14, 124.25 (6 C), 124.40, 131.21, 134.86, 134.91 (6 C), 134.98, 135.24, 137.61, 138.84, 141.67, 144.22, 183.90, 184.75; LRMS (CI), m/e 863 (M++1) (1), 487 (2), 235 (2), 211 (3), 205 (2), 198 (6), 197 (100), 81 (11), 70 (12); HRMS calcd. For $C_{59}H_{90}O_4$: 862.6839, found 862.6836; IR(neat) 3435,1615,1612, 1447, 1384, 1263, 1204, 1150, 1103, 876 cm^{-1}.

2-(3-Methyl-2-heptenyl)-3-methyl-[1,4]-naphthoquinone: Representative Procedure: To a solution of Me_3Al (0.17g, 2.4 mmol) and Cl_2ZrCp_2 (0.15 g, 0.5 mmol) in 1,2-dichloroethane (2 mL) was added at 23 °C 1-hexyne (99 mg, 1.2 mmol). The reaction mixture was stirred for 4 h at 23 °C. To this reaction mixture were successively added at 0 °C THF (10 mL), 2-chloromethyl-3-methyl-[1,4]-naphthoquinone[d] (0.22 g, 1 mmol), and $Pd(PPh_3)_4$ (23 mg, 0.02 mmol). The reaction mixture was stirred for 1 h at 23 °C, diluted with Et_2O, quenched with 1 N HCl (added dropwise), and extracted with Et_2O. The combined organic layers were dried over $MgSO_4$, concentrated *in vacuo*. NMR analysis of the crude mixture indicated the formation of the title compound in 97% yield. Flash chromatography (hexane/ethylacetate = 10:1) afforded 0.26 g (93%) of the title compound as an yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ 0.82 (t, J = 7.0 Hz, 3 H), 1.1-1.4 (m, 4 H), 1.74 (s, 3 H), 1.93 (t, J = 6.7 Hz, 2 H), 2.14 (s, 3 H), 3.32 (d, J = 7.0 Hz, 2 H), 4.9-5.1 (m, 1 H), 7.5-7.7 (m, 2 H), 7.9-8.1 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$, Me_4Si) δ 12.60, 13.92, 16.24, 22.29, 25.92, 30.01, 39.36, 118.72, 126.09, 126.21, 132.06, 132.10, 133.18, 133.23, 137.81, 143.26, 146.12, 184.41, 185.35; HRMS calcd. For $C_{19}H_{22}O_2$ 282.1620, found 282.1618.

Coenzyme Q_3[e]: This compound was prepared according to the procedure described above from 6,10-dimethyl-5,9-undecadien-1-yne, prepared by disilylation of 1-trimethylsilyl-6,10-dimethyl-5,9-undecadien-1-yne[f] with TBAF, and 2-chloromethyl-5,6-dimethoxy-3-methyl-[1,4]-benzoquinone[d] in 82% yiled; ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ 1.51(s, 3 H), 1.53 (s, 3H), 1.61 (s, 3 H), 1.68 (s, 3 H), 1.8-2.1 (m, 11 H), 3.12 (d, J = 6.7 Hz, 2 H), 3.92 (s, 3 H), 3.93 (s, 3 H), 4.8-5.1 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, Me_4Si) δ 11.79, 15.89, 16.19, 17.53, 25.19, 25.56, 26.63, 39.57, 39.59, 60.98 (2 C), 118.84, 123.76, 124.21, 131.12, 135.04, 137.42, 138.72, 141.55, 144.14, 144.27, 183.76, 184.61.

Menaquinone-3[d]: This compound was prepared according to the procedure described above from 6,10-dimethyl-5,9-undecadien-1-yne, prepared by disilylation of 1-trimethylsilyl-

6,10-dimethyl-5,9-undecadien-1-yne[f] with TBAF, and 2-chloromethyl-3-methyl-[1,4]-naphthoquinone[d] in 89% yiled; ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ 1.51(s, 3 H), 1.53 (s, 3H), 1.61 (s, 3 H), 1.68 (s, 3 H), 1.8-2.1 (m, 11 H), 3.12 (d, J = 6.7 Hz, 2 H), 3.92 (s, 3 H), 3.93 (s, 3 H), 4.8-5.1 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, Me_4Si) δ 11.79, 15.89, 16.19, 17.53, 25.19, 25.56, 26.63, 39.57, 39.59, 60.98 (2 C), 118.84, 123.76, 124.21, 131.12, 135.04, 137.42, 138.72, 141.55, 144.14, 144.27, 183.76, 184.61.

(*Z*)-8-Iodo-6-methyl-1-trimethylsilyl-5-octen-1-yne (10): 4-Bromo-1-trimethylsilyl-1-butyne (4.1 g, 20 mmol) was treated with a mixture of Mg (0.72 g, 30 mmol) and flame-dried $ZnBr_2$ (4.51 g, 20 mmol) in THF (40 mL) at 50 °C for 12 h,[g] and the supernatant was transferred into another dry flask under Ar atmosphere. To this solution were added (*Z*)-1,4-diiodo-2-methylbut-1-ene (**1b**) (4.83 g, 15 mmol) and $Cl_2Pd(dppf)(CH_2Cl_2)$ (0.25 g, 0.3 mmol) at 23 °C. The reaction mixture was stirred at 23 °C for 12 h, quenched with saturated aqueous NH_4Cl, extracted with hexanes, washed with $NaHCO_3$, brine, dried over $MgSO_4$, and evaporated. The crude product was purified by flash column chromatography (hexanes) to give the title compound **10**: 4.02 g (84%); >98% *Z*; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.12 (s, 9 H), 1.69 (s, 3 H), 2.05-2.15 (m, 4 H), 2.61 (t, J = 7.9 Hz, 2 H), 3.15 (t, J = 8.1 Hz, 2 H), 5.29 (t, J = 6.6 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.12 (3 C), 3.38, 20.21, 22.59, 27.24, 36.38, 84.73, 106.87, 126.04, 134.96; HRMS calcd. For $C_{12}H_{21}SiI$ 320.0457, found 320.0462.

1-Iodo-2-methyl-propene:[h] This compound was prepared by the Cl_2ZrCp_2-catalyzed methylalumination of propyne followed by iodinolysis according to the general procedure reported previously[i] in 60% yield; ^{1}H NMR (200 MHz, $CDCl_3$, Me_4Si) δ 1.85 (s, 3 H), 1.91 (d, J = 1.4 Hz, 3 H), 5.8-5.85 (m, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 25.26, 25.35, 73.95, 144.12.

(Z)-6,10-Dimethyl-5,9-undecadien-1-yne (11):[j] To a solution of **10** (1.6 g, 5 mmol) in 15 mL of Et_2O was added dropwise at -78 °C a 1.7 M solution of *t*-BuLi (6.5 mL, 11 mmol) in pentane, and the reaction mixture was stirred at -78 °C for 45 min. A solution of anhydrous

$ZnBr_2$ (1.13 g, 5 mmol) in THF (20 mL) and DMF (20 mL) was transferred into the reaction mixture at -78 °C using a double-tipped needle, and the mixture was stirred at -78 °C for 5 min and then warmed to 0 °C. 1-Iodo-2-methylpropene (1.09 g, 6 mmol), $Pd_2(dba)_3$ (0.12 g, 0.13 mmol), and tris(2-furyl)phosphine (0.12 g, 0.5 mmol) were added successively. The resultant mixture was stirred at 23 °C for 3 h, quenched with aqueous NH_4Cl, extracted with Et_2O, dried over $MgSO_4$, and evaporated. The crude product was filtered through a short column packed with silica gel, washed with hexanes, and treated with 0.2 M KOH in MeOH-H_2O (95:5) at 23 °C for 3 h. Usual workup and distillation gave the title compound **11** as a colorless liquid: 0.69 g, 78% yiled; >98% stereomeric purity; ^{1}H NMR (200 MHz, $CDCl_3$, Me_4Si) δ 1.59 (s, 3 H), 1.66 (s, 3 H), 1.68 (s, 3H), 1.92 (t, J = 2.6 Hz, 1 H), 2.0-2.1 (m, 4 H), 2.15-2.2 (m, 4 H), 5.0-5.2 (m, 2 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 17.61, 19.08, 23.34, 25.67, 26.56, 27.03, 32.00, 68.15, 84.47, 123.22, 124.14, 131.64, 138.81.

(2*E*, 6*Z*)-3,7,11-Trimethyl-2,6,10-dodecatrien-1-ol[k] (7): This compound was prepared from **11** according our previously reported procedure[l] in 71% yield; >98 stereisomeric purity; ^{1}H NMR (200 MHz, $CDCl_3$, Me_4Si) δ 1.61 (s, 3 H), 1.68 (bs, 9 H), 1.85 (bs, 1 H), 1.95-2.2 (m, 8 H), 4.13 (d, J = 7.0 Hz, 2 H), 5.15-5.2 (m, 2 H), 5.41 (t, J = 7.9 Hz, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 16.15, 17.53, 23.27, 25.62, 26.09, 26.48, 31.87, 39.74, 59.15, 123.32, 124.18, 124.50, 131.44, 135.36, 139.36.

(2*Z*, 6*Z*)-3,7,11-Trimethyl-2,6,10-dodecatrien-1-ol[k] (**8**): Alkyne **11** was treated successively with 1 molar equiv of *n*-BuLi in THF at -78 °C for 15 min and 3 molar equiv of paraformaldehyde at 23 °C for 3 h. The reaction mixture was quenched with aqueous NH_4Cl, extracted with Et_2O, washed with $NaHCO_3$ and brine, and evaporated. The crude product was purified by flash column chromatography (hexanes/ethyl acetate = 5:1) to give (*Z*)-7,11-dimethyl-6,10-dodecadien-2-yn-1-ol in 86% yield; >98% stereoisomeric purity; ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ 1.62 (d, J = 0.8 Hz, 3 H), 1.7 (s, 3 H), 1.72 (d, J = 1.1 Hz, 3 H), 2.0-2.15 (m, 4

H), 2.2-2.4 (m, 5 H), 4.13 (bs, 2 H), 5.1-5.25 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.65, 19.46, 23.40, 25.71, 26.62, 27.22, 32.05, 51.24, 78.52, 86.23, 123.45, 124.20, 131.73, 136.80. (*Z*)-7,11-Dimethyl-6,10-dodecadien-2-yn-1-ol was converted to (2*Z*, 6*Z*)-3,7,11-trimethyl-2,6,10-dodecatrien-1-ol[k] (**8**) according to the literature procedure[m] in 81% yield; >98% stereoisomeric purity; ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ 1.61 (s, 3 H), 1.69 (bs, 6 H), 1.74 (s, 3 H), 1.85 (bs, 1 H), 2.0-2.15 (m, 8 H), 4.08 (d, *J* = 7.0 Hz, 2 H), 5.05-5.15 (m, 2 H), 5.43 (dt, *J* = 7.0, 1.4 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.64, 23.34, 23.48, 25.72, 26.40, 26.67, 31.97, 32.30, 58.90, 124.26, 124.60, 124.66, 131.60, 136.03, 139.47.

Lithiation of (*Z*)-8-Iodo-6-methyl-1-trimethylsilyl-5-octen-1-yne (10): Compound **10** was treated with *t*-BuLi in ether at -78 °C for 45 min as described above. Protonolysis of the lithiated compound **12** produced 6-methyl-1-trimethylsilyl-5-nonaen-1-yne[n] in quantitative yield judged by GC analysis of the crude mixture. Deuterolysis produced deutered compounds (8*d*)- 6-methyl-1-trimethylsilyl-5-nonaen-1-yne in quantitative GC yield with >95% D incorporation. After lithiation of **10**, the reaction mixture was treated with a solution of dry $ZnBr_2$ in THF for 5 min at -78 °C and then 3 h at 23 °C for 3 h, protonolysis and deuterolysis gave the same results as above.

6-Methyl-1-trimethylsilyl-5-nonaen-1-yne:[n] ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.12 (s, 9 H), 0.95 (t, *J* = 7.6 HZ, 3 H), 1.67 (s, 3 H), 2.02 (q, *J* = 7.6 Hz, 2 H), 2.15-2.25 (m, 4 H), 5.05-5.15 (m, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 0.14 (3 C), 12.92, 20.57, 22.84, 24.83, 27.12, 84.32, 107.42, 122.35, 138.65.

(8*d*)- 6-Methyl-1-trimethylsilyl-5-nonaen-1-yne: ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ 0.12 (s, 9 H), 0.85-1.0 (m, 2 H), 1.66 (s, 3 H), 2.00 (t, *J* = 7.7 Hz, 2 H), 2.15-2.25 (m, 4 H), 5.0-5.15 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.12 (3 C), 12.03 (t, *J* = 19.5 HZ), 20.56, 22.64, 24.73, 27.12, 84.28, 107.39, 122.31, 138.62.

Stability of the Lithio Derivative 12: Compound **10** was lithiated as described above. The reaction mixture was warmed to 23 °C over 1 h. Protonolysis of the reaction mixture gave two products which were separated by column chromatography (hexanes), 6-methyl-1-trimethylsilyl-5-nonaen-1-yne (51% yield) and 6-methyl-1-trimethylsilyl-1,2,5-nonatriene (40% yield). Deuterolysis gave (3*d*)- 6-methyl-1-trimethylsilyl-5-nonaen-1-yne in 48% yiled with >95% D incorporation and (1*d*)-6-methyl-1-trimethylsilyl-1,2,5-nonatriene in 37% yield with ~100% D incorporation.

6-Methyl-1-trimethylsilyl-1,2,5-nonatriene: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.06 (s, 9 H), 0.94 (t, J = 7.6 HZ, 3 H), 1.67 (s, 3 H), 2.01 (q, J = 7.5 Hz, 2 H), 2.6-2.7 (m, 2 H), 4.7-4.8 (m, 1 H), 4.85-4.95 (m, 1H), 5.05-5.15 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ -0.97 (3 C), 12.80, 22.82, 24.75, 26.17, 82.89, 83.05, 122.22, 137.76, 210.12.

(3*d*)- 6-Methyl-1-trimethylsilyl-5-nonaen-1-yne: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.12 (s, 9 H), 0.95 (t, J = 7.6 HZ, 3 H), 1.67 (s, 3 H), 2.02 (q, J = 7.6 Hz, 2 H), 2.05-2.15 (m, 3 H), 5.08 (t, J = 6.4 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.13 (3 C), 12.91, 20.29 (t, J = 20.0 Hz), 22.83, 24.82, 27.03, 84.32, 107.40, 122.34, 138.62.

(1*d*)-6-Methyl-1-trimethylsilyl-1,2,5-nonatriene: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.07 (s, 9 H), 0.95 (t, J = 7.6 HZ, 3 H), 1.67 (s, 3 H), 2.02 (q, J = 7.5 Hz, 2 H), 2.64 (t, J = 6.9 Hz, 2 H), 4.75 (t, J = 6.7 Hz, 1 H), 5.11 (t, J = 7.4 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ -0.97 (3 C), 12.79, 22.80, 24.77, 26.20, 83.02, 122.27, 137.75, 210.24.

(5*Z*, 9*E*)-12-Iodo-6,10-dimethyl-1-trimethylsilyl-5,9-dodecadien-1-yne: To a solution of (*Z*)-8-iodo-6-methyl-1-trimethylsilyl-5-octen-1-yne (**10**) (1.6 g, 5.0 mmol) in Et_2O (15 mL) was added dropwise at -78 °C a 1.7 M solution of *t*-BuLi (6.5 mL, 11.1 mmol) in pentane, and the mixture was stirred for 45 min. A solution of dry $ZnBr_2$ (1.13 g, 5.0 mmol) in THF (30 mL) was added using a double-tipped needle at -78 °C. The reaction mixture was stirred at -78 °C for 5 min and then warmed to 0 °C. A solution prepared from $Cl_2Pd(dppf)(CH_2Cl_2)$ (0.41 g, 0.5 mmol)

and diisobutylaluminum hydride (0.14 g, 1.0 mmol) in THF (10 mL) was added to the reaction mixture at 0 °C, followed by **1a** (1.91 g, 5.9 mmol). The mixture was stirred at 23 °C for 1 h, quenched with aqueous NH_4Cl, extracted with Et_2O, washed with aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and evaporated. The crude product was purified by flash column chromatography (hexanes) to give the titled compound as a colorless oil: 1.57 g, 81% yield; >98% stereoisomeric purity; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.14 (s, 9 H), 1.62 (s, 3 H), 1.70 (s, 3 H), 2.0-2.1 (m, 4 H), 2.15-2.25 (m, 4 H), 2.52 (t, J = 7.4 Hz, 2 H), 3.2 (t, J = 7.8 Hz, 2 H), 5.1-5.3 (m, 2 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 0.13 (3 C), 4.78, 15.28, 20.48, 23.36, 26.52, 27.24, 31.64, 43.79, 84.37, 107.23, 123.59, 126.99, 133.68, 136.23; HRMS calcd. For $C_{17}H_{29}SiI$ 388.1083, found 388.1071.

(5Z, 9E)-6,10,14-Trimethyl-5,9,13-pentadecatrien-1-yne: This compound was prepared according to the procedure described above for the synthesis of **11** in 67% yield; >98% stereoisomeric purity; ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ 1.59 (bs, 6 H), 1.66 (s, 3 H), 1.69 (s, 3 H), 1.9-2.1 (m, 9 H), 2.15-2.3 (m, 4 H), 5.05-5.2 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.23, 17.93, 19.37, 23.64, 25.94, 26.76, 26.96, 27.33, 32.26, 39.98, 68.45, 84.74, 123.48, 124.24, 124.61, 131.55, 135.56, 137.16; HRMS calcd. For $C_{18}H_{28}$ 244.2191, found 244.2191.

(2*Z*, 6*Z*, 10*E*)-3,7,11,15-Tetramethyl-2,6,10,14-hexadecatetraen-1-ol (9): This compound was prepared from (5*Z*, 9*E*)-6,10,14-trimethyl-5,9,13-pentadecatrien-1-yne in 73% yield according to our previously reported procedure[1]; >98% stereoisomeric purity; ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ 1.52 (bs, 1 H), 1.60 (bs, 6 H), 1.68 (m, 9 H), 1.95-2.1 (m, 12 H), 4.14 (d, J = 6.9 Hz, 2 H), 5.0-5.1 (m, 3 H), 5.41 (dt, J = 6.9, 1.1 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.89, 16.19, 17.59, 23.31, 25.59, 26.13, 26.44, 26.64, 31.89, 39.67, 39.78, 59.25, 123.38, 124.03, 124.30, 124.49, 131.20, 135.10, 135.46, 139.48; HRMS calcd. For $C_{20}H_{34}O$ 290.2610, found 290.2623.

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