Supporting Information for:

Addition of Dithiols to Bis-Ynones: Development of a Versatile Platform for the Synthesis of Polyketide Natural Products

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Supporting Information

Materials and methods

All non-aqueous reactions were carried out in oven-dried glassware under an argon atmosphere, unless otherwise noted. All solvents were reagent grade. Diethyl ether and tetrahydrofuran were freshly distilled from sodium benzophenone ketyl under argon. Dichloromethane was freshly distilled from calcium hydride. Pentan-3-one was distilled before use. All other commercially available reagents were used as received.

Except as indicated otherwise, reactions were magnetically stirred and monitored by thin layer chromatography (TLC) with precoated glass-backed plates (Merck Kieselgel 60 F254) and visualized by UV fluorescence ($\lambda = 254$ nm) or by staining with acidic ammonium molybdate (IV) or acidic potassium permanganate (VII) and developed with appropriate heating. Flash chromatography was performed with Merck Kieselgel (230-400 mesh). Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated.

Optical rotations were measured on a Perkin-Elmer Model 343 polarimeter with a sodium lamp and are reported as follows: $[\alpha]_D^{25}$, $[c$ (g/100 mL), solvent]. Infrared spectra were recorded with a Perkin Elmer Spectrum One FT-IR and are reported in cm^{-1} (abs). Proton magnetic resonance spectra (^1H NMR) were recorded at 400 or 600 MHz on a Bruker DPX400 NMR or a Bruker Advance DRX600 instrument respectively and are reported as follows: chemical shift δ in ppm, (multiplicity, coupling constant J in Hz, number of protons, assignment). Residual protic solvent was used as the internal reference, taking chloroform as δ 7.26. Carbon magnetic resonance spectra (^{13}C NMR) were recorded at 100 or 150 MHz on a Bruker DPX400 NMR or a Bruker Advance DRX600 instrument respectively. Chemical shifts are quoted in ppm and referenced to the appropriate solvent peak, taking chloroform as δ 77.0. The spectra are assigned as fully as possible using the locants derived from the compound name. High-resolution mass spectra were obtained on a Kratos MS890MS spectrometer using electron impact (EI) or fast atom bombardment (+FAB) techniques, or a Kratos Q-TOF spectrometer using electrospray (+ESI) at the Department of Chemistry, University of Cambridge. Microanalyses were determined in the microanalytical laboratories at the University of Cambridge Chemical Laboratories, Lensfield Road, Cambridge, CB2 1EW.

Preparative Experiments

1-(*tert*-Butyl-diphenyl-silanyloxy)-hex-5-yne

To a solution of 5-hexyn-1-ol (2.00 g, 20.38 mmol) and imidazole (3.33 g, 48.91 mmol) in tetrahydrofuran (70 mL) was added *tert*-butyl-diphenyl-silyl chloride (TBDPSCI) (5.88 g, 21.40 mmol). After stirring at ambient temperature for 16 h, the reaction mixture was filtered through a pad of silica and concentrated under reduced pressure. Gradient flash

chromatography (Petroleum ether/diethyl ether, 100:0 → 90:10) afforded the alkyne (5.22 g, 76%) as a clear colorless oil: TLC R_f = 0.91 (10% Et₂O/P.E.); IR (thin film) 3309 (m), 2932 (s), 2858 (s), 1473 (m), 1428 (s), 1100 (s), 823 (m), 740 (m), 702 (s) cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.66-7.68 (m, 4 H, PhH₄), 7.36-7.42 (m, 6 H, PhH₆), 3.68 (t, J = 5.8 Hz, 2 H, C₁-H₂), 2.18-2.21 (m, 2 H, C₄-H₂), 1.93 (t, J = 2.5 Hz, 1 H, C₆-H), 1.62-1.69 (m, 4 H, C₂-H₂ and C₃-H₂), 1.05 (s, 9 H, OSiPh₂C(CH₃)₃); spectra consistent with known data.¹

7-(*tert*-Butyl-diphenyl-silanyloxy)-hept-2-ynal

To a solution of 1-(*tert*-butyl-diphenyl-silanyloxy)-hex-5-yne (3.93 g, 11.67 mmol) in tetrahydrofuran (80 mL) at -78 °C was added *n*BuLi (1.6 M in hexane) (4.67 mL, 11.67 mmol) dropwise. After stirring at -78 °C for 1 h, LiBr (1.22 g, 14.00 mmol) was added, followed by DMF (4.51 mL, 58.34 mmol) dropwise over 10 min. After stirring at -78 °C for a further 30 min. the reaction mixture was allowed to warm to 0 °C over 16 h, then quenched by the slow addition of saturated aqueous NH₄Cl (20 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (3 × 20 mL). The combined organic extracts were washed with H₂O (1 × 20 mL), and brine (1 × 20 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 → 90:10) afforded the ynal (3.43 g, 81%) as a clear, colorless oil: TLC R_f = 0.60 (10% Et₂O/P.E.); IR (neat) 2934 (m), 2858 (m), 2238 (m), 1688 (s), 1472 (m), 1428 (s), 1280 (m), 1111 (s), 823 (m), 741 (m), 702 (s) cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.17 (s, 1 H, C₁-H), 7.67-7.69 (m, 4 H, PhH₄), 7.38-7.42 (m, 6 H, PhH₆), 3.71 (t, J = 6.0 Hz, 2 H, C₇-H₂), 2.43 (t, J = 6.5 Hz, 2 H, C₄-H₂), 1.69-1.73 (m, 4 H, C₅-H₂, C₆-H₂), 1.08 (s, 9 H, OSiPh₂C(CH₃)₃); ¹³C NMR (100 MHz, CDCl₃) δ 177.1 (C), 135.5 (Ph), 133.8 (Ph), 129.6 (Ph), 127.7 (Ph), 99.0 (C), 81.8 (C₂), 63.1 (C₇), 31.5 (C₅), 26.9 (OSiPh₂C(CH₃)₃), 24.2 (C₆), 19.2 (OSiPh₂C(CH₃)₃), 18.9 (C₄); high resolution mass spectrum (+ESI) m/z 364.1872 [(M+Na)⁺; calcd for C₂₃H₂₈O₂NaSi: 364.1859].

1-(*tert*-Butyl-diphenyl-silanyloxy)-trideca-5,8-diyn-7-ol

To a solution of hex-1-yne (0.45 g, 5.49 mmol) in tetrahydrofuran (50 mL) at -78 °C was added *n*BuLi (1.6 M in hexane) (2.07 mL, 5.49 mmol) dropwise. After stirring at -78 °C for 1 h, 7-(*tert*-butyl-diphenyl-silanyloxy)-hept-2-ynal (2.00 g, 5.49 mmol) was added dropwise over 10 min. After stirring at -78 °C for a further 2 h, the reaction mixture was quenched by the slow addition of saturated aqueous NH₄Cl (10 mL). The layers were

¹ De Oliveira Imbroisi, D.; Simpkins, N. S. *J. Chem. Soc. Perkin Trans. I* **1991**, 1815.

separated, and the aqueous phase was extracted with ethyl acetate (2 × 50 mL). The combined organic extracts were washed with H₂O (1 × 20 mL), and brine (1 × 20 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 → 90:10) afforded the bis-ynol (1.07 g, 44%) as a clear, colorless oil: ¹H NMR (400 MHz, CDCl₃) δ 7.65-7.67 (m, 4 H, PhH₄), 7.36-7.42 (m, 6 H, PhH₆), 5.08 (dqn, *J* = 7.2, 3.0 Hz, 1 H, C₇-H), 3.68 (t, *J* = 5.9 Hz, 2 H, C₁-H₂), 2.17-2.25 (m, 4 H, C₂-H₂, C₃-H₂), 2.00 (d, *J* = 7.2 Hz, 1 H, C₇-OH), 1.60-1.67 (m, 4 H, C₁₁-H₂, C₁₂-H₂), 1.47-1.52 (m, 2 H, C₄-H₂), 1.37-1.46 (m, 2 H, C₁₀-H₂), 1.05 (s, 9 H, OSiPh₂C(CH₃)₃), 0.90 (t, *J* = 7.2 Hz, 3 H, C₁₃-H₃).

1-(*tert*-Butyl-diphenyl-silanyloxy)-trideca-5,8-diyn-7-one (3a).

To a solution of 1-(*tert*-butyl-diphenyl-silanyloxy)-trideca-5,8-diyn-7-ol (1.05g, 2.34 mmol) in dichloromethane (50 mL) were added 4 Å molecular sieves (1.17 g), 4-methylmorpholine *N*-oxide (0.41 g, 3.52 mmol) and tetrapropylammonium perruthenate (TPAP) (82 mg, 0.23 mmol). The reaction mixture was stirred at ambient temperature for 1 h. The crude reaction mixture was filtered through a plug of silica, washed with diethyl ether (100 mL) and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 → 95:5) afforded **3a** (0.75 g, 72%) as a yellow oil: TLC R_f = 0.58 (10% Et₂O/P.E.); IR (neat) 2931 (s), 2859 (s), 2206 (s), 1715 (m), 1625 (s), 1472 (m), 1428 (s), 1389 (m), 1361 (m), 1325 (m), 1241 (s), 1187 (m), 1107 (s), 1008 (s), 997 (s), 822 (s), 740 (s), 723 (s), 700 (s) cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.66 (dd, *J* = 7.7, 1.5 Hz, 4 H, PhH₄), 7.36-7.42 (m, 6 H, PhH₆), 3.68 (t, *J* = 5.7 Hz, 2 H, C₁-H₂), 2.37-2.41 (m, 4 H, C₂-H₂, C₃-H₂), 1.61-1.75 (m, 4 H, C₁₀-H₂, C₁₁-H₂), 1.58 (t, *J* = 7.5 Hz, 2 H, C₄-H₂), 1.39-1.48 (m, 2 H, C₁₂-H₂), 1.05 (s, 9 H, OSiPh₂C(CH₃)₃), 0.92 (t, *J* = 7.3 Hz, 3 H, C₁₃-H₃); ¹³C NMR (100 MHz, CDCl₃) δ 161.8 (C₇), 135.9 (Ph), 134.3 (Ph), 130.0 (Ph), 128.1 (Ph), 95.1 (C₅), 94.8 (C₉), 82.8 (C₆), 82.7 (C₈), 63.5 (C₁), 31.9 (C₂), 29.9, 27.3 (C₁₁), 24.6 (OSiPh₂C(CH₃)₃), 22.4 (C₁₂), 19.6 (C₄), 19.3 (C₁₀), 19.2 (C₃), 13.8 (C₁₃), 1.0 (OSiPh₂C(CH₃)₃); high resolution mass spectrum (+ESI) *m/z* 467.2382 [(M+Na)⁺; calcd for C₂₉H₃₆O₂NaSi: 467.2380].

1-(*tert*-Butyl-diphenyl-silanyloxy)-5-([1,3]dithian-2-yl)-9-([1,3]dithian-2-yl)-trideca-7-one (4a).

To a solution of 1-(*tert*-butyl-diphenyl-silanyloxy)-trideca-5,8-diyn-7-one (**3a**) (50 mg, 0.11 mmol) and propane-1,3-dithiol (27 mg, 0.25 mmol) in tetrahydrofuran (3 mL) and methanol (1.5 mL) stirred at -10 °C for 30 min. was added sodium hydroxide (10 mg, 0.25 mmol). The reaction mixture was allowed to warm to ambient temperature over 20 h. The reaction mixture was quenched with saturated aqueous NH₄Cl solution (5 mL).

The layers were separated, and the aqueous phase was extracted with diethyl ether (3×5 mL). The combined organic extracts were washed with H_2O (1×5 mL), and brine (1×5 mL), dried over MgSO_4 , filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 $\rightarrow$ 90:10) afforded **4a** (67 mg, 90%) as a clear, pale yellow oil: TLC R_f = 0.13 (10% $\text{Et}_2\text{O}/\text{P.E.}$); IR (neat) 3071 (w), 2930 (s), 2857 (s), 1717 (s), 1564 (m), 1462 (m), 1427 (s), 1389 (m), 1339 (m), 1276 (m), 1239 (m), 1188 (m), 1107 (s), 998 (s), 939 (m), 908 (m), 869 (m), 822 (s), 740 (s), 701 (s), 687 (s); ^1H NMR (400 MHz, CDCl_3) δ 7.66-7.67 (m, 4 H, PhH_4), 7.36-7.45 (m, 6 H, PhH_6), 3.68 (t, J = 5.5 Hz, 2 H, $\text{C}_1\text{-H}_2$), 3.14 (m, 4 H, $\text{C}_6\text{-H}_2$ and $\text{C}_8\text{-H}_2$), 2.78-2.93 (m, 8 H, both of $\text{SCH}_2\text{CH}_2\text{CH}_2\text{S}$), 2.04-2.10 (m, 4 H, C_4H_2 and $\text{C}_{10}\text{-H}_2$), 2.00-2.02 (m, 2 H, one of $\text{SCH}_2\text{CH}_2\text{CH}_2\text{S}$), 1.89-1.97 (m, 2 H, one of $\text{SCH}_2\text{CH}_2\text{CH}_2\text{S}$), 1.56-1.60 (m, 4 H, $\text{C}_2\text{-H}_2$ and $\text{C}_3\text{-H}_2$), 1.46-1.52 (m, 2 H, $\text{C}_{11}\text{-H}_2$), 1.34 (qn, J = 7.3 Hz, 2 H, $\text{C}_{12}\text{-H}_2$), 1.05 (s, 9 H, $\text{OSiPh}_2\text{C}(\text{CH}_3)_3$), 0.92 (t, J = 7.3 Hz, 3 H, $\text{C}_{13}\text{-H}_3$); ^{13}C NMR (100 MHz, CDCl_3) δ 202.5 (C_7), 135.6 (Ph), 134.1 (Ph), 129.5 (Ph), 127.6 (Ph), 63.7 (C_1), 51.0 (C_6), 50.6 (C_8), 50.6 (C_9), 50.5 (C_5), 38.4 (C_{10}), 38.3 (C_4), 32.6 (C_2), 26.9 (C_{11}), 26.5 ($\text{OSiPh}_2\text{C}(\text{CH}_3)_3$), 26.4 ($\text{SCH}_2\text{CH}_2\text{CH}_2\text{S}$), 25.0 ($\text{SCH}_2\text{CH}_2\text{CH}_2\text{S}$), 22.8 (C_{12}), 19.2 (C_3), 14.0 (C_{13}), 1.0 ($\text{OSiPh}_2\text{C}(\text{CH}_3)_3$); high resolution mass spectrum (+ESI) m/z 683.2517 [$(\text{M}+\text{Na})^+$; calcd for $\text{C}_{35}\text{H}_{52}\text{O}_2\text{S}_4\text{SiNa}$: 683.2504].

1-(*tert*-Butyl-dimethyl-silanyloxy)-but-3-yne

To a solution of 3-butyne-1-ol (9.26 g, 132.1 mmol) and imidazole (21.59 g, 317.1 mmol) in tetrahydrofuran (200 mL) was added *tert*-butyl-dimethyl-silyl chloride (TBSCl) (23.90 g, 158.5 mmol). After stirring at ambient temperature for 3 h, the reaction mixture was filtered through a pad of silica and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 $\rightarrow$ 90:10) afforded the alkyne (24.62 g, 100%) as a clear colorless oil: IR (neat) 3315 (m), 2955 (s), 2930 (s), 2858 (s), 1473 (s), 1386 (m), 1362 (m), 1255 (s), 1102 (s), 1060 (s), 1006 (s), 939 (m), 915 (s), 834 (s), 775 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 3.75 (t, J = 7.1 Hz, 2 H, $\text{C}_1\text{-H}_2$), 2.40 (td, J = 7.1, 2.6 Hz, 2H, $\text{C}_2\text{-H}_2$), 1.96 (t, J = 2.6 Hz, 1 H, $\text{C}_4\text{-H}$), 0.90 (s, 9 H, $\text{OSi}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$), 0.08 (s, 6 H, $\text{OSi}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$); spectra consistent with known data.²

5-(*tert*-Butyl-dimethyl-silanyloxy)-pent-2-ynal

To a solution of 1-(*tert*-butyl-dimethyl-silanyloxy)-but-3-yne (10.00 g, 52.24 mmol) in tetrahydrofuran (500 mL) stirred at -78°C for 30 min. was added a solution of *n*BuLi (1.6 M in hexane) (47.46 mL, 75.94 mmol). The reaction mixture was stirred at -78°C for 1 h. To the reaction mixture was added a solution of *N*-formylmorpholine (8.74 g,

² Germain, J.; Deslongchamps, P. *J. Org. Chem.* **2002**, 67, 5269

7.64 mmol) in tetrahydrofuran (50 mL). The reaction mixture was allowed to warm to ambient temperature over 2 h. The reaction mixture was quenched with saturated solution of aqueous NH_4Cl (300 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (3×200 mL). The combined organic extracts were washed with H_2O (1×200 mL), and brine (1×200 mL), dried over MgSO_4 , filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 $\rightarrow$ 97:3) afforded the ynal (7.38 g, 64%) as a yellow oil: TLC R_f = 0.58 (10% $\text{Et}_2\text{O}/\text{P.E.}$); IR (neat) 3256 (m), 2955 (s), 2930 (s), 2885 (s), 2857 (s), 2225 (s), 2098 (s), 1634 (s), 1472 (s), 1386 (m), 1362 (m), 1329 (m), 1253 (s), 1207 (s), 1106 (s), 1056 (m), 1006 (s), 984 (m), 939 (m), 909 (s), 835 (s), 810 (s), 776 (s), 725 (s), 684 (s), 661 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 9.18 (s, 1 H, $\text{C}_1\text{-H}$), 3.80 (t, J = 6.7 Hz, 2 H, $\text{C}_5\text{-H}_2$), 2.63 (t, J = 6.7 Hz, 2 H, $\text{C}_4\text{-H}_2$), 0.90 (s, 9 H, $\text{OSi}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$), 0.09 (s, 6 H, $\text{OSi}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$); ^{13}C NMR (100 MHz, CDCl_3) δ 176.9 (C_1), 96.1 (C_3), 82.3 (C_2), 60.6 (C_5), 25.8 ($\text{OSi}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$), 23.5 (C_4), 18.3 ($\text{OSi}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$), -5.4 ($\text{OSi}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$); high resolution mass spectrum (+ESI) m/z 235.1130 [$(\text{M}+\text{Na})^+$; calcd for $\text{C}_{11}\text{H}_{20}\text{O}_2\text{Na}$: 235.1130].

1-(*tert*-Butyl-dimethyl-silanyloxy)-8-(tetrahydro-pyran-2-yloxy)-octa-3,6-diyn-5-ol

To a solution of 2-prop-2-ynyloxy-tetrahydro-pyran (0.66g, 4.71 mmol) in tetrahydrofuran (50 mL) stirred at -78 $^{\circ}\text{C}$ for 30 min. was added a solution of $n\text{BuLi}$ (1.6 M in hexane) (2.21 mL, 3.53 mmol). The reaction mixture was stirred at -78 $^{\circ}\text{C}$ for 1 h. The reaction mixture was treated with a solution of 5-(*tert*-butyl-dimethyl-silanyloxy)-pent-2-ynal (0.50 g, 2.35 mmol) in tetrahydrofuran (10 mL). The reaction mixture was stirred at -78 $^{\circ}\text{C}$ for 2 h. The reaction mixture was quenched with saturated solution of aqueous NH_4Cl (50 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (3×50 mL). The combined organic extracts were washed with H_2O (1×50 mL), and brine (1×50 mL), dried over MgSO_4 , filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 $\rightarrow$ 90:10 $\rightarrow$ 80:20 $\rightarrow$ 70:30) afforded the bis-ynol (0.66 g, 80%) as a clear yellow oil: TLC R_f = 0.06 (10% $\text{Et}_2\text{O}/\text{P.E.}$); IR (neat) 3397 (br, m), 2929 (s), 2856 (s), 1472 (s), 1442 (s), 1389 (s), 1361 (s), 1299 (s), 1254 (s), 1202 (s), 1184 (s), 1152 (s), 1103 (s), 1079 (s), 1055 (s), 1023 (s), 945 (s), 903 (s), 834 (s), 812 (s), 776 (s), 731 (s), 663 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 5.13 (d, J = 6.8 Hz, 1 H, $\text{C}_5\text{-H}$), 4.80 (t, J = 3.4 Hz, 1 H, THP), 4.34 (dd, J = 15.8, 1.8 Hz, 1 H, one of $\text{C}_8\text{-H}_2$), 4.26 (dd, J = 15.8, 1.9 Hz, 1 H, one of $\text{C}_8\text{-H}_2$), 3.80-3.86 (m, 1 H, THP), 3.73 (t, J = 7.1 Hz, 2 H, $\text{C}_1\text{-H}_2$), 3.51-3.56 (m, 1 H, THP), 2.44 (dt, J = 7.1, 2.1 Hz, 2 H, $\text{C}_2\text{-H}_2$), 1.69-1.84 (m, 2 H, THP), 1.51-1.65 (m, 4 H, THP), 0.89 (s, 9 H, $\text{OSi}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$), 0.07 (s, 6 H, $\text{OSi}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$); ^{13}C NMR (100 MHz, CDCl_3) δ 96.9 (OTHP), 83.4 (C_7), 82.6 (C_3), 80.3 (C_6), 78.4 (C_4), 61.9 (OTHP), 61.5 (C_1), 54.2 (C_8), 52.3 (C_5), 30.2 (OTHP), 25.9 ($\text{OSi}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$), 25.3 (OTHP), 23.1 (C_2), 18.9 (OTHP), 18.3 ($\text{OSi}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$), -

5.3 (OSi(CH₃)₂C(CH₃)₃); high resolution mass spectrum (+ESI) m/z 375.1968 [(M+Na)⁺; calcd for C₁₉H₃₂O₄NaSi: 375.1968].

1-(*tert*-Butyl-dimethyl-silanyloxy)-8-(tetrahydro-pyran-2-yloxy)-octa-3,6-diyn-5-one (3b).

To a solution of 1-(*tert*-butyl-dimethyl-silanyloxy)-8-(tetrahydro-pyran-2-yloxy)-octa-3,6-diyn-5-ol (0.50g, 1.42 mmol) in dichloromethane (30 mL) were added 4 Å molecular sieves (1 g), 4-methylmorpholine *N*-oxide (0.25 g, 2.13 mmol) and TPAP (50 mg, 0.14 mmol). The reaction mixture was stirred at ambient temperature for 1 h. The crude reaction mixture was filtered through a plug of silica, washed with diethyl ether (100 mL) and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 → 90:10) afforded **3b** (0.16 g, 64%) as a clear yellow oil: TLC R_f = 0.30 (20% Et₂O/P.E.); IR (neat) 2930 (s), 2857 (s), 2215 (s), 1631 (s), 1472 (m), 1442 (m), 1388 (m), 1361 (m), 1329 (m), 1236 (s), 1202 (s), 1184 (m), 1112 (s), 1078 (s), 1057 (s), 1030 (s), 958 (s), 941 (s), 904 (s), 871 (s), 836 (s), 814 (s), 777 (s), 730 (s) cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 4.80 (t, J = 3.3 Hz, 1 H, OTHP), 4.43 (s, 2 H, C₈-H₂), 3.83 (m, 1 H, OTHP), 3.80 (t, J = 6.7 Hz, 2 H, C₁-H₂), 3.54 (m, 1 H, OTHP), 2.61 (t, J = 6.7 Hz, 2 H, C₂-H₂), 1.78 (m, 2 H, OTHP), 1.58 (m, 4 H, OTHP), 0.90 (s, 9 H, OSi(CH₃)₂C(CH₃)₃), 0.09 (s, 6 H, OSi(CH₃)₂C(CH₃)₃); ¹³C NMR (100 MHz, CDCl₃) δ 160.4 (C₅), 97.3 (THP), 93.0 (C₃), 88.2 (C₆), 85.7 (C₇), 82.5 (C₄), 62.0 (THP), 60.5 (C₁), 53.8 (C₈), 30.1 (THP), 25.8 (OSi(CH₃)₂C(CH₃)₃), 25.2 (THP), 23.6 (C₂), 18.8 (OSi(CH₃)₂C(CH₃)₃), 18.3 (THP), -5.4 (OSi(CH₃)₂C(CH₃)₃); high resolution mass spectrum (+ESI) m/z 373.1811 [(M+Na)⁺; calcd for C₁₉H₃₀O₄NaSi: 373.1811]; elemental analysis C, 64.84%; H, 8.59%.

1-(*tert*-Butyl-dimethyl-silanyloxy)-3-([1,3]dithian-2-yl)-7-([1,3]dithian-2-yl)-8-(tetrahydropyran-2-yloxy)-octan-5-one (4b).

To a solution of 1-(*tert*-butyl-dimethyl-silanyloxy)-8-(tetrahydro-pyran-2-yloxy)-octa-3,6-diyn-5-one (**3b**) (100 mg, 0.29 mmol) and propane-1,3-dithiol (68 mg, 0.63 mmol) in dichloromethane (1 mL) and methanol (4 mL) stirred at -10 °C for 30 min. was added sodium methoxide (34 mg, 0.63 mmol). The reaction mixture was allowed to warm to ambient temperature over 20 h. The reaction mixture was quenched with saturated aqueous NH₄Cl solution (10 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (3 × 10 mL). The combined organic extracts were washed with H₂O (1 × 10 mL), and brine (1 × 10 mL), dried over MgSO₄, filtered and

concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 → 95:5 → 90:10 → 80:20) afforded **4b** (150 mg, 89%) as a yellow oil: TLC R_f = 0.50 (50% Et₂O/P.E.); IR (neat) 2929 (s), 2855 (m), 2248 (w), 1715 (m), 1471 (m), 1424 (m), 1387 (m), 1349 (m), 1277 (m), 1254 (m), 1201 (m), 1184 (m), 1120 (s), 1076 (s), 1032 (s), 1004 (m), 976 (s), 907 (s), 869 (s), 835 (s), 814 (s), 776 (s), 728 (s), 661 (s) cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 4.72 (t, J = 3.2 Hz, 1 H, OTHP), 4.17 (d, J = 10.5 Hz, 1 H, one of C₈-H₂), 3.91 (m, 1 H, OTHP), 3.88 (d, J = 10.5 Hz, 1 H, one of C₈-H₂), 3.86 (t, J = 7.0 Hz, 2 H, C₁-H₂), 3.51 (m, 1 H, OTHP), 3.19 (s, 2 H, C₄-H₂), 3.11 (d, J = 3.5 Hz, 2 H, C₆-H₂), 2.97 (m, 2 H, SCH₂CH₂CH₂S), 2.86 (m, 4 H, SCH₂CH₂CH₂S), 2.76 (m, 2 H, SCH₂CH₂CH₂S), 2.36 (t, J = 7.0 Hz, 2 H, C₂-H₂), 1.97 (m, 4 H, SCH₂CH₂CH₂S), 1.81 (m, 1 H, OTHP), 1.61 (m, 5 H, OTHP), 0.88 (s, 9H, OSi(CH₃)₂C(CH₃)₃), 0.06 (s, 6H, OSi(CH₃)₂C(CH₃)₃); ¹³C NMR (100 MHz, CDCl₃) δ 202.1 (C₅), 98.8 (OTHP), 70.3 (C₈), 62.0 (OTHP), 59.7 (C₁), 51.9 (OTHP), 50.9 (C₄), 50.1 (C₆), 48.8 (OTHP), 40.7 (C₂), 30.3 (OTHP), 26.4 (SCH₂CH₂CH₂S), 26.3 (SCH₂CH₂CH₂S), 26.1 (SCH₂CH₂CH₂S), 26.0 (SCH₂CH₂CH₂S), 25.4 (OSi(CH₃)₂C(CH₃)₃), 24.9 (SCH₂CH₂CH₂S), 24.8 (SCH₂CH₂CH₂S), 24.8 (OTHP), 19.1 (OTHP), 18.3 (OSi(CH₃)₂C(CH₃)₃), -5.3 (OSi(CH₃)₂C(CH₃)₃); high resolution mass spectrum (+ESI) m/z 589.1946 [(M+Na)⁺; calcd for C₂₅H₄₆O₄SiNa: 589.1946].

1-(*tert*-Butyl-dimethyl-silanyloxy)-7-phenyl-hepta-3,6-diyn-5-ol

To a solution of ethynyl benzene (0.48g, 4.71 mmol) in tetrahydrofuran (50 mL) stirred at -78 °C for 30 min. was added a solution of *n*BuLi (1.6 M in hexane) (2.21 mL, 3.53 mmol). The reaction mixture was stirred at -78 °C for 1 h. The reaction mixture was treated with a solution of 5-(*tert*-butyl-dimethyl-silanyloxy)-pent-2-ynal (0.50 g, 2.35 mmol) in tetrahydrofuran (10 mL). The reaction mixture was stirred at -78 °C for 2 h, then quenched with aqueous NH₄Cl (50 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (3 × 50 mL). The combined organic extracts were washed with H₂O (1 × 50 mL), and brine (1 × 50 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 → 98:2 → 96:4 → 94:6 → 90:10) afforded the bis-ynol (0.60 g, 81%) as a clear yellow oil: TLC R_f = 0.19 (10% Et₂O/P.E.); IR (neat) 3399 (br, m), 2953 (s), 2928 (s), 2856 (s), 2236 (w), 1682 (w), 1599 (w), 1490 (s), 1472 (s), 1444 (s), 1387 (s), 1362 (s), 1334 (m), 1301 (s), 1253 (s), 1220 (m), 1136 (s), 1100 (s), 1056 (s), 1030 (s), 1015 (s), 998 (s), 976 (s), 952 (s), 910 (s), 834 (s), 809 (s), 776 (s), 755 (s), 733 (s), 690 (s), 665 (s) cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.47 (m, 2 H, PhH₂), 7.28-7.36 (m, 3 H, PhH₃), 5.33 (dt, J = 7.3, 2.0 Hz, 1 H, C₅-H), 3.76 (t, J = 7.0 Hz, 2 H, C₁-H₂), 2.49 (dt, J = 7.0, 2.0 Hz, 2 H, C₂-H₂), 2.34 (d, J = 7.3 Hz, 1 H, C₅OH), 0.90 (s, 9 H, OSi(CH₃)₂C(CH₃)₃), 0.09 (s, 6 H, OSi(CH₃)₂C(CH₃)₃); ¹³C NMR (100 MHz, CDCl₃) δ 131.8 (Ph), 128.7 (Ph), 128.3 (Ph), 122.1 (Ph), 86.5 (C₆), 84.0 (C₇), 82.8 (C₃), 78.5 (C₄), 61.5 (C₁), 52.8 (C₅), 25.9 (OSi(CH₃)₂C(CH₃)₃), 23.2 (C₂), 18.3 (OSi(CH₃)₂C(CH₃)₃),

-5.3 (OSi(CH₃)₂C(CH₃)₃); high resolution mass spectrum (+ESI) m/z 337.1600 [(M+Na)⁺; calcd for C₁₉H₂₆O₂NaSi: 337.1600]; elemental analysis C, 72.70%; H, 8.31%.

1-(*tert*-Butyl-dimethyl-silanyloxy)-7-phenyl-hepta-3,6-diyn-5-one (3c).

To a solution of 1-(*tert*-butyl-dimethyl-silanyloxy)-7-phenyl-hepta-3,6-diyn-5-ol (0.20g, 0.64 mmol) in dichloromethane (15 mL) were added 4 Å molecular sieves (0.5 g), 4-methylmorpholine *N*-oxide (0.11 g, 0.94 mmol) and TPAP (22 mg, 0.06 mmol). The reaction mixture was stirred at ambient temperature for 1 h. The crude reaction mixture was filtered through a plug of silica, washed with diethyl ether (50 mL) and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 → 80:20) afforded **3c** (0.16 g, 82%) as a clear yellow oil: TLC R_f = 0.50 (20% Et₂O/P.E.); IR (neat) 2955 (m), 2929 (m), 2857 (m), 2198 (s), 1622 (s), 1490 (m), 1472 (m), 1444 (m), 1383 (m), 1362 (m), 1329 (m), 1284 (s), 1253 (s), 1183 (s), 1172 (s), 1108 (s), 1056 (m), 1027 (s), 1012 (s), 997 (s), 909 (s), 835 (s), 809 (s), 777 (s), 757 (s), 737 (s), 716 (s), 688 (s), 660 (s) cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.60 (d, J = 7.4 Hz, 2 H, PhH₂), 7.48 (t, J = 7.4 Hz, 1 H, PhH), 7.39 (t, J = 7.4 Hz, 2 H, PhH₂), 3.84 (t, J = 6.7 Hz, 2 H, C₁-H₂), 2.66 (t, J = 6.7 Hz, 2 H, C₂-H₂), 0.91 (s, 9 H, OSi(CH₃)₂C(CH₃)₃), 0.11 (s, 6 H, OSi(CH₃)₂C(CH₃)₃); ¹³C NMR (100 MHz, CDCl₃) δ 160.9 (C₅), 133.3 (Ph), 131.1 (Ph), 128.6 (Ph), 119.6 (Ph), 92.7 (C₃), 90.7 (C₇), 89.3 (C₆), 82.8 (C₄), 60.6 (C₁), 25.8 (OSi(CH₃)₂C(CH₃)₃), 23.6 (C₂), 18.3 (OSi(CH₃)₂C(CH₃)₃), -5.3 (OSi(CH₃)₂C(CH₃)₃); high resolution mass spectrum (+ESI) m/z 335.1443 [(M+Na)⁺; calcd for C₁₉H₂₄O₂NaSi: 335.1443]; elemental analysis C, 72.78%; H, 7.67%.

1-(*tert*-Butyl-dimethyl-silanyloxy)-3-([1,3]dithian-2-yl)-7-([1,3]dithian-2-yl)-7-phenyl-heptan-5-one (4c).

To a solution of 1-(*tert*-butyl-dimethyl-silanyloxy)-7-phenyl-hepta-3,6-diyn-5-one (**3c**) (100 mg, 0.32 mmol) and propane-1,3-dithiol (76 mg, 0.70 mmol) in dichloromethane (1 mL) and methanol (4 mL) stirred at -10 °C for 30 min. was added sodium methoxide (38 mg, 0.70 mmol). The reaction mixture was allowed to warm to ambient temperature over 20 h. The reaction mixture was quenched with saturated aqueous NH₄Cl solution (10 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (3 × 10 mL). The combined organic extracts were washed with H₂O (1 × 10 mL), and brine (1 × 10 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 → 95:5 → 94:6 → 93:7 → 92:8) afforded **4c** (136 mg, 80%) as a yellow oil: R_f = 0.75 (50% Et₂O/P.E.); IR

(neat) 2929 (s), 2856 (s), 2250 (w), 1710 (s), 1471 (m), 1443 (s), 1423 (s), 1389 (m), 1340 (m), 1277 (s), 1251 (s), 1090 (s), 1035 (s), 1004 (s), 908 (s), 835 (s), 776 (s), 729 (s), 700 (s), 662 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.95 (d, $J = 7.5$ Hz, 2 H, PhH_2), 7.40 (t, $J = 7.5$ Hz, 2 H, PhH_2), 7.29 (t, $J = 7.5$ Hz, 1 H, PhH), 3.74 (t, $J = 7.1$ Hz, 2 H, $\text{C}_1\text{-H}_2$), 3.24 (s, 2 H, $\text{C}_6\text{-H}_2$), 2.78 (s, 2 H, $\text{C}_4\text{-H}_2$), 2.67 (m, 8 H, $\text{SCH}_2\text{CH}_2\text{CH}_2\text{S}$), 2.20 (t, $J = 7.1$ Hz, 2 H, $\text{C}_2\text{-H}_2$), 1.95 (m, 2 H $\text{SCH}_2\text{CH}_2\text{CH}_2\text{S}$), 1.87 (m, 2 H, $\text{SCH}_2\text{CH}_2\text{CH}_2\text{S}$), 0.87 (s, 9 H, $\text{OSi}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$), 0.03 (s, 6 H, $\text{OSi}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$); ^{13}C NMR (100 MHz, CDCl_3) δ 201.0 (C_5), 140.8 (Ph), 128.7 (Ph), 128.6 (Ph), 127.6 (Ph), 59.5 (C_1), 58.0 (C_6), 55.2 (C_7), 51.5 (C_4), 48.6 (C_3), 40.9 (C_2), 27.7 ($\text{SCH}_2\text{CH}_2\text{CH}_2\text{S}$), 27.7 ($\text{SCH}_2\text{CH}_2\text{CH}_2\text{S}$), 26.4 ($\text{SCH}_2\text{CH}_2\text{CH}_2\text{S}$), 26.4 ($\text{SCH}_2\text{CH}_2\text{CH}_2\text{S}$), 26.0 ($\text{OSi}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$), 24.7 ($\text{SCH}_2\text{CH}_2\text{CH}_2\text{S}$), 24.6 ($\text{SCH}_2\text{CH}_2\text{CH}_2\text{S}$), 18.3 ($\text{OSi}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$), -5.3 ($\text{OSi}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$); high resolution mass spectrum (+ESI) m/z 551.1578 [(M+Na) $^+$]; calcd for $\text{C}_{25}\text{H}_{40}\text{O}_2\text{S}_4\text{SiNa}$: 551.1578].

1-(*tert*-Butyl-dimethyl-silanyloxy)-hepta-3,6-diyn-5-ol

To a solution of 5-(*tert*-butyl-dimethyl-silanyloxy)-pent-2-ynal (1.00 g, 4.71 mmol) in tetrahydrofuran (10 mL) stirred at -78°C for 30 min. was added a solution of ethynylmagnesium bromide (0.5 M in tetrahydrofuran) (18.8 mL, 9.42 mmol). The reaction mixture was allowed to warm to -30°C and stirred for 2 h. The reaction mixture was quenched with saturated solution of aqueous NH_4Cl (10 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (3×10 mL). The combined organic extracts were washed with H_2O (1×10 mL), and brine (1×10 mL), dried over MgSO_4 , filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 $\rightarrow$ 95:5 $\rightarrow$ 90:10) afforded the bisynol (0.83 g, 74%) as a clear yellow oil: TLC R_f = 0.07 (5% $\text{Et}_2\text{O}/\text{P.E.}$); IR (neat) 3312 (br, m), 2955 (s), 2930 (s), 2857 (s), 1472 (s), 1386 (s), 1362 (m), 1297 (m), 1254 (s), 1139 (s), 1100 (s), 1057 (s), 1023 (s), 972 (m), 914 (s), 835 (s), 809 (s), 776 (s), 660 (s) cm^{-1} ; ^1H NMR (600 MHz, CDCl_3) δ 5.09 (dd, $J = 7.4, 2.2$ Hz, 1 H, $\text{C}_5\text{-H}$), 3.74 (t, $J = 7.0$ Hz, 2 H, $\text{C}_1\text{-H}_2$), 2.54 (d, $J = 2.2$ Hz, 1 H, $\text{C}_7\text{-H}$), 2.46 (dt, $J = 7.0, 2.2$ Hz, 2 H, $\text{C}_2\text{-H}_2$), 2.17 (d, $J = 7.4$ Hz, 1 H, C_5OH), 0.90 (s, 9 H, $\text{OSi}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$), 0.08 (s, 6 H, $\text{OSi}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$); ^{13}C NMR (150 MHz, CDCl_3) δ 83.0 (C_4), 81.3 (C_3), 78.0 (C_5), 72.3 (C_7), 61.4 (C_1), 52.1 (C_6), 25.9 ($\text{OSi}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$), 23.1 (C_2), 18.3 ($\text{OSi}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$), -5.3 ($\text{OSi}(\text{CH}_3)_2\text{C}(\text{CH}_3)_3$); high resolution mass spectrum (+ESI) m/z 261.1287 [(M+Na) $^+$]; calcd for $\text{C}_{13}\text{H}_{22}\text{O}_2\text{SiNa}$: 261.1287].

1-(*tert*-Butyl-dimethyl-silanyloxy)-hepta-3,6-diyn-5-one (3d).

To a solution of 1-(*tert*-butyl-dimethyl-silanyloxy)-hepta-3,6-diyn-5-ol (1.04 g, 4.35 mmol) in dichloromethane (50 mL) stirred at 0°C for 30 min. was added Dess-Martin

periodinane (2.77 g, 6.52 mmol). The reaction mixture was allowed to warm to ambient temperature and stirred for 2 h. The reaction mixture was quenched with a 1:1 solution of saturated aqueous Na₂S₂O₃ and saturated aqueous NaHCO₃ (50 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (3 × 50 mL). The combined organic extracts were washed with H₂O (1 × 50 mL), and brine (1 × 50 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 → 95:5 → 90:10) afforded **3d** (0.94 g, 92%) as a clear yellow oil: TLC R_f = 0.42 (5% Et₂O/P.E.); IR (neat) 2955 (m), 2929 (m), 2884 (m), 2857 (m), 2227 (m), 2097 (m), 1634 (s), 1472 (m), 1386 (w), 1362 (w), 1329 (w), 1254 (s), 1207 (s), 1106 (s), 1056 (m), 1006 (s), 984 (m), 939 (w), 909 (m), 835 (s), 810 (s), 777 (s), 725 (s), 683 (s), 661 (s) cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 3.81 (t, *J* = 6.6 Hz, 2 H, C₁-H₂), 3.26 (s, 1 H, C₇-H), 2.63 (t, *J* = 6.6 Hz, 2 H, C₂-H₂), 0.90 (s, 9 H, OSi(CH₃)₂C(CH₃)₃), 0.09 (s, 6 H, OSi(CH₃)₂C(CH₃)₃); ¹³C NMR (100 MHz, CDCl₃) δ 160.2 (C₅), 93.8 (C₃), 82.5 (C₄), 82.2 (C₆), 78.2 (C₇), 60.5 (C₁), 25.8 (OSi(CH₃)₂C(CH₃)₃), 23.6 (C₂), 18.3 (OSi(CH₃)₂C(CH₃)₃), -5.4 (OSi(CH₃)₂C(CH₃)₃); high resolution mass spectrum (+ESI) *m/z* 259.1130 [(M+Na)⁺; calcd for C₁₃H₂₀O₂SiNa: 259.1130].

1-([1,3]Dithian-2-yl)-5-([1,3]dithian-2-yl)-7-(*tert*-butyl-dimethyl-silanyloxy)-heptan-3-one (4d).

To a solution of 1-(*tert*-butyl-dimethyl-silanyloxy)-hepta-3,6-diyn-5-one (**3d**) (100 mg, 0.42 mmol) and propane-1,3-dithiol (101 mg, 0.93 mmol) in dichloromethane (2 mL) and methanol (2 mL) stirred at -10 °C for 30 min. was added sodium hydroxide (37 mg, 0.93 mmol). The reaction mixture was stirred for 30 min. The reaction mixture was quenched with saturated aqueous NH₄Cl solution (5 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (3 × 5 mL). The combined organic extracts were washed with H₂O (1 × 5 mL), and brine (1 × 5 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 → 90:10 → 80:20) afforded **4d** (181 mg, 94%) as a clear pale yellow oil: TLC R_f = 0.70 (50% Et₂O/P.E.); IR (neat) 2950 (m), 2927 (m), 2897 (m), 2855 (m), 1717 (m), 1471 (m), 1422 (m), 1346 (m), 1276 (m), 1251 (s), 1173 (m), 1086 (s), 1005 (m), 968 (m), 939 (m), 908 (s), 834 (s), 776 (s), 731 (s), 663 (s) cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 4.50 (t, *J* = 6.9 Hz, 1 H, C₁-H), 3.86 (t, *J* = 6.8 Hz, 2 H, C₇-H₂), 3.12 (s, 2 H, C₄-H₂), 2.93 (m, 2 H, two of SCH₂CH₂CH₂S), 2.92 (d, *J* = 6.9 Hz, 2 H, C₂-H₂), 2.84 (m, 6 H, six of SCH₂CH₂CH₂S), 2.36 (t, *J* = 6.8 Hz, 2 H, C₆-H₂), 2.08 (m, 1 H, one of SCH₂CH₂CH₂S), 1.88 (m, 2 H, two of SCH₂CH₂CH₂S), 1.85 (m, 1 H, one of SCH₂CH₂CH₂S), 0.89 (s, 9 H, OSi(CH₃)₂C(CH₃)₃), 0.06 (s, 6 H, OSi(CH₃)₂C(CH₃)₃); ¹³C NMR (100 MHz, CDCl₃) δ 201.7 (C), 59.7 (C₇), 59.7 (C₅), 51.2 (C₄), 49.7 (one of SCH₂CH₂CH₂S), 48.7 (C₂), 41.2 (C₁), 40.8 (C₆), 30.2 (one of SCH₂CH₂CH₂S), 26.5 (one of SCH₂CH₂CH₂S), 26.0 (one of SCH₂CH₂CH₂S), 25.3 (OSi(CH₃)₂C(CH₃)₃), 24.8 (one of SCH₂CH₂CH₂S), 24.8 (one of SCH₂CH₂CH₂S), 18.3 (OSi(CH₃)₂C(CH₃)₃), -5.3

(OSi(CH₃)₂C(CH₃)₃); high resolution mass spectrum (+ESI) m/z 475.1265 [(M+Na)⁺; calcd for C₁₉H₃₆O₂S₄SiNa: 475.1265].

2 (R) 3-Benzoyloxy-2-methyl-propionaldehyde

Under argon, a solution of oxalyl chloride (7.04 g, 55.48 mmol) was stirred in dichloromethane (100 mL) at –78 °C for 30 min. To this solution was added dropwise dimethyl sulfoxide (DMSO) (10.84 g, 138.70 mmol). The reaction mixture was stirred at –78 °C for 10 min., and a solution of 2 (S), 3-benzyloxy-2-methyl-propan-1-ol (5.00 g, 27.74 mmol) in dichloromethane (20 mL) was added dropwise. The reaction mixture was stirred at –78 °C for 25 min., then *N,N*-diisopropylthylamine (DIPEA) (14.34 g, 110.96 mmol) was added slowly and the reaction mixture was stirred at –78 °C for 25 min., then allowed to warm to –10 °C and stirred for 25 min. The reaction mixture was quenched with a solution of pH7 phosphate buffer (100 mL). The reaction mixture was poured into diethyl ether (400 mL), washed with a saturated solution of NH₄Cl (100 mL), water (100 mL) and brine (100 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 → 95:5 → 90:10 → 85:15 → 80:20) afforded the aldehyde (4.22 g, 77%) as a clear pale yellow oil: TLC R_f = 0.26 (10% Et₂O/P.E.); [α]_D²⁵ –0.8 (*c* 1.055, CHCl₃); IR (neat) 2860 (m), 2719 (w), 1721 (s), 1496 (m), 1454 (s), 1361 (m), 1247 (w), 1204 (m), 1094 (s), 1028 (s), 915 (m), 806 (m), 736 (s), 697 (s) cm^{–1}; ¹H NMR (600 MHz, CDCl₃) δ 9.74 (d, *J* = 1.1 Hz, 1 H, C₁-H), 7.32 (m, 5 H, Ph-H₅), 4.53 (s, 2 H, CH₂Ph), 3.69 (dd, *J* = 9.4, 6.8 Hz, 1 H, one of C₃-H₂), 3.65 (dd, *J* = 9.4, 5.2 Hz, 1 H, one of C₃-H₂), 2.67 (m, 1 H, C₂-H), 1.14 (d, *J* = 7.1 Hz, 3 H, C₂CH₃); ¹³C NMR (150 MHz, CDCl₃) 203.8 (C₁), 137.9 (Ph), 128.4 (Ph), 127.7 (Ph), 127.6 (Ph), 73.3 (CH₂Ph), 70.1 (C₃), 46.8 (C₂), 10.7 (C₂CH₃); high resolution mass spectrum (+ESI) m/z 178.0985 [M⁺]; calcd for C₁₁H₁₄O₂: 178.2277]; spectra consistent with known data.³

3 (S) 1,1-Dibromo-3-methyl-5-benzyloxybut-1-ene

To a solution of triphenylphosphine (10.61 g, 40.40 mmol) and carbon tetrabromide (6.70 g, 20.20 mmol) in dichloromethane (100 mL) stirred at 0 °C for 5 min. was added a solution of 2 (R), 3-benzyloxy-2-methyl-propionaldehyde (2.00 g, 10.10 mmol) in dichloromethane (10 mL). The reaction mixture was stirred at 0 °C for 10 min. The reaction mixture was quenched with saturated solution of aqueous K₂CO₃. The layers were separated, and the aqueous phase was extracted with dichloromethane (3 × 50 mL). The combined organic extracts were washed with H₂O (1 × 50 mL), and brine (1 × 50

³ Meyers, A. I.; Babiak, K. A.; Campbell, A. L.; Comins, D. L.; Fleming, M. P.; Henning, R.; Heuschmann, M.; Hudspeth, J. P.; Kane, J. M.; Reider, P. J.; Roland, D. M.; Shimizu, K.; Tomioka, K.; Walkup R. D. *J. Am. Chem. Soc.* **1983**, *105*, 5015

mL), dried over MgSO_4 , filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 $\rightarrow$ 95:5) afforded the dibromo-olefin (3.00 g, 89%) as a colorless oil: TLC R_f = 0.74 (10% $\text{Et}_2\text{O}/\text{P.E.}$); $[\alpha]_D^{25}$ +21.6 (c 1.04, CHCl_3); IR (neat) 3030 (w), 2964 (m), 2931 (m), 2854 (s), 2066 (w), 1616 (m), 1496 (s), 1453 (s), 1358 (s), 1233 (s), 1204 (s), 1096 (s), 1028 (s), 973 (m), 923 (m), 906 (m), 843 (m), 783 (s), 734 (s), 697 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.34 (m, 5 H, PhH_5), 6.33 (d, J = 9.1 Hz, 1 H, $\text{C}_3\text{-H}$), 4.53 (d, J = 2.0 Hz, 2 H, CH_2Ph), 3.39 (m, 2 H, $\text{C}_1\text{-H}_2$), 2.80 (m, 1 H, $\text{C}_2\text{-H}$), 1.08 (d, J = 6.8 Hz, 3 H, C_2CH_3); ^{13}C NMR (100 MHz, CDCl_3) 141.2 (C_3), 138.3 (C_2), 128.4 (Ph), 127.7 (Ph), 127.5 (Ph), 88.9 (C_4), 73.1 (CH_2Ph), 73.0 (C_1), 38.8 (C_2), 15.9 (C_2CH_3); high resolution mass spectrum (+ESI) m/z 333.9379 [M^+ ; calcd for $\text{C}_{12}\text{H}_{14}\text{OBr}_2$: 333.9370]; elemental analysis C, 43.43%; H, 4.30%.

4 (S) 5-Benzyloxy-4-methyl-pent-2-ynal

To a solution of 3 (S) 1,1-dibromo-3-methyl-5-benzyloxybut-1-ene (2.00 g, 5.99 mmol) in tetrahydrofuran (100 mL) stirred at -78°C for 30 min., was added a solution of $n\text{BuLi}$ (1.6 M in hexane) (9.36 mL, 14.97 mmol). The reaction mixture was stirred at -78°C for 1 h. To the reaction mixture was added a solution of N -formylmorpholine (0.97 g, 8.38 mmol) in tetrahydrofuran (5 mL). The reaction mixture was allowed to warm to ambient temperature over 2 h. The reaction mixture was quenched with saturated solution of aqueous NH_4Cl (100 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (3×50 mL). The combined organic extracts were washed with H_2O (1×50 mL), and brine (1×50 mL), dried over MgSO_4 , filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 $\rightarrow$ 95:5 $\rightarrow$ 90:10) afforded the ynal (0.51 g, 42%) as a colorless oil: TLC R_f = 0.33 (10% $\text{Et}_2\text{O}/\text{P.E.}$); $[\alpha]_D^{25}$ -24.2 (c 1.07, CHCl_3); IR (neat) 3032 (w), 2860 (s), 2211 (s), 1663 (s), 1496 (m), 1454 (s), 1388 (m), 1360 (m), 1334 (m), 1260 (m), 1203 (m), 1164 (s), 1119 (s), 1096 (s), 1028 (s), 957 (m), 887 (s), 793 (s), 739 (s), 699 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 9.20 (d, J = 0.7 Hz, 1 H, $\text{C}_1\text{-H}$), 7.35 (m, 5 H, PhH_5), 4.57 (s, 2 H, CH_2Ph), 3.56 (dd, J = 9.1, 6.6 Hz, 1 H, one of $\text{C}_5\text{-H}_2$), 3.46 (dd, J = 9.1, 6.6 Hz, 1 H, one of $\text{C}_5\text{-H}_2$), 2.96 (q, J = 6.8 Hz, 1 H, $\text{C}_4\text{-H}$), 1.28 (d, J = 7.0 Hz, 3 H, C_4CH_3); ^{13}C NMR (100 MHz, CDCl_3) δ 177.0 (C_1), 137.8 (Ph), 128.5 (Ph), 127.8 (Ph), 127.7 (Ph), 100.0 (C_3), 81.9 (C_2), 73.2 (CH_2Ph), 72.7 (C_5), 27.3 (C_4), 16.6 (C_4CH_3); high resolution mass spectrum (+ESI) m/z 202.0999 [M^+ ; calcd for $\text{C}_{13}\text{H}_{14}\text{O}_2$: 202.0994]; elemental analysis C, 77.14%; H, 7.02%.

2 (S) 1-Benzyloxy-2-methyl-hepta-3,6-diyn-5-ol

To a solution of 4 (*S*) 5-benzyloxy-4-methyl-pent-2-ynal (0.51 g, 2.53 mmol) in tetrahydrofuran (20 mL) stirred at -78 °C for 30 min. was added a solution of ethynylmagnesium bromide (0.5 M in tetrahydrofuran) (20.26 mL, 10.13 mmol). The reaction mixture was allowed to warm to -30 °C and stirred for 30 min. The reaction mixture was quenched with saturated solution of aqueous NH₄Cl (10 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (3 × 10 mL). The combined organic extracts were washed with H₂O (1 × 10 mL), and brine (1 × 10 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 → 90:10 → 70:30) afforded the bis-ynol (0.41 g, 72%) as a clear yellow oil: TLC R_f = 0.05 (10% Et₂O/P.E.); IR (neat) 3285 (br, m), 3032 (m), 2974 (m), 2864 (m), 2243 (w), 2122 (w), 1496 (m), 1454 (s), 1362 (s), 1298 (s), 1205 (m), 1166 (m), 1123 (s), 1092 (s), 1074 (s), 1017 (s), 919 (s), 781 (m), 736 (s), 697 (s) cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 7.35 (m, 5H, PhH₅), 5.10 (d, *J* = 6.5 Hz, 1 H, C₅-H), 4.57 (s, 2 H, CH₂Ph), 3.53 (dd, *J* = 9.1, 6.3 Hz, 1 H, one of C₁-H₂), 3.39 (dd, *J* = 8.9, 8.9 Hz, 1 H, one of C₁-H₂), 2.80 (m, 1 H, C₂-H), 2.54 (m, 1 H, C₇-H), 1.22 (d, *J* = 6.9 Hz, 3 H, C₂CH₃); ¹³C NMR (150 MHz, CDCl₃) δ 138.1 (Ph), 138.1 (Ph'), 128.4 (Ph), 127.7 (Ph), 127.6 (Ph), 87.3 (C₃), 81.4 (C₇), 78.0 (C₄), 73.5 (C₁), 73.0 (CH₂Ph), 72.2 (C₆), 72.2 (C'₆), 52.1 (C₅), 26.7 (C₂), 17.3 (C₂CH₃); high resolution mass spectrum (+ESI) *m/z* 251.1048 [(M+Na)⁺; calcd for C₁₅H₁₆O₂Na: 251.1048].

2 (*S*) 1-Benzyloxy-2-methyl-hepta-3,6-diyn-5-one (3e).

To a solution of 2 (*S*) 1-benzyloxy-2-methyl-hepta-3,6-diyn-5-ol (200 mg, 0.88 mmol) in dichloromethane (5 mL) stirred at 0 °C for 30 min. was added Dess-Martin periodinane (0.56 g, 1.31 mmol). The reaction mixture was allowed to warm to ambient temperature and stirred for 1 h. The reaction mixture was quenched with a 1:1 solution of saturated aqueous Na₂S₂O₃ and saturated aqueous NaHCO₃ (10 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (3 × 10 mL). The combined organic extracts were washed with H₂O (1 × 10 mL), and brine (1 × 10 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 → 90:10 → 80:20) afforded **3e** (123 mg, 62%) as a clear yellow oil: TLC R_f = 0.42 (20% Et₂O/P.E.); ¹H NMR (400 MHz, CDCl₃) δ 7.35 (m, 5 H, Ph-H₅), 4.58 (s, 2 H, CH₂Ph), 3.57 (dd, *J* = 9.1, 6.5 Hz, 1 H, one of C₁-H₂), 3.47 (dd, *J* = 9.1, 6.8 Hz, 1 H, one of C₁-H₂), 3.27 (s, 1 H, C₇-H), 2.96 (m, 1 H, C₂-H), 1.29 (d, *J* = 7.0 Hz, 3 H, C₂CH₃).

6 (*R*) 1-([1,3]Dithian-2-yl)-5-([1,3]dithian-2-yl)-6-methyl-7-benzyloxy-heptan-3-one (4e).

To a solution of 2 (*S*) 1-benzyloxy-2-methyl-hepta-3,6-diyn-5-one (**3e**). (190 mg, 0.84 mmol) and propane-1,3-dithiol (200 mg, 1.85 mmol) in dichloromethane (8 mL) and methanol (8 mL) stirred at -10 °C for 30 min. was added sodium methoxide (100 mg, 1.85 mmol). The reaction mixture was allowed to warm to ambient temperature over 18 h. The reaction mixture was quenched with saturated aqueous NH₄Cl solution (10 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (3 × 10 mL). The combined organic extracts were washed with H₂O (1 × 10 mL), and brine (1 × 10 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 → 90:10 → 80:20 → 70:30 → 60:40) afforded **4e** (314 mg, 84%) as a yellow oil: TLC R_f = 0.47 (50% Et₂O/P.E.); [α]_D²⁵ +30.6 (*c* 1.10, CHCl₃); IR (neat) 2898 (s), 1717 (s), 1496 (m), 1452 (s), 1421 (s), 1346 (s), 1276 (s), 1242 (s), 1173 (m), 1088 (s), 1027 (s), 984 (s), 907 (s), 870 (m), 815 (m), 733 (s), 698 (s), 676 (m) cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.33 (m, 4 H, PhH₄), 7.27 (m, 1 H, PhH), 4.52 (d, *J* = 11.7 Hz, 1 H, one of CH₂Ph), 4.48 (t, *J* = 7.0 Hz, 1 H, C₁-H), 4.47 (d, *J* = 11.7 Hz, 1 H, one of CH₂Ph), 3.96 (dd, *J* = 9.4, 4.3 Hz, 1 H, one of C₇-H₂), 3.48 (dd, *J* = 9.4, 7.3 Hz, 1 H, one of C₇-H₂), 3.29 (d, *J* = 15.6 Hz, 1 H, one of C₄-H₂), 3.15 (d, *J* = 15.6 Hz, 1 H, one of C₄-H₂), 2.89 (m, 2 H, C₂-H₂), 2.79 (m, 7 H, SCH₂CH₂CH₂S), 2.68 (m, 1 H, C₆-H), 2.08 (m, 1 H, one of SCH₂CH₂CH₂S), 2.00 (m, 1 H, one of SCH₂CH₂CH₂S), 1.89 (m, 1 H, one of SCH₂CH₂CH₂S), 1.87 (m, 1 H, one of SCH₂CH₂CH₂S), 1.25 (d, *J* = 6.9 Hz, 3 H, C₆CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 202.2 (C₃), 138.5 (Ph), 128.3 (Ph), 127.6 (Ph), 127.4 (Ph), 73.0 (CH₂Ph), 72.2 (C₇), 53.8 (C₅), 49.6 (C₂), 49.2 (C₄), 41.3 (C₁), 40.1 (C₆), 30.2 (one of SCH₂CH₂CH₂S), 26.4 (one of SCH₂CH₂CH₂S), 26.4 (one of SCH₂CH₂CH₂S), 26.2 (one of SCH₂CH₂CH₂S), 25.3 (one of SCH₂CH₂CH₂S), 24.7 (one of SCH₂CH₂CH₂S), 13.5 (C₆CH₃); high resolution mass spectrum (+ESI) *m/z* 465.1026 [(M+Na)⁺; calcd for C₂₁H₃₀O₂S₄Na: 465.1026].

4(*R*)-2-(2,2-Diethyl-[1,3]dioxolan-4-yl)-ethanol

To a solution of (*R*)-1,2,4-butanetriol (**5**) (6.76 g, 63.68 mmol) in freshly distilled pentan-3-one (320 mL) was added *p*-toluenesulfonic acid (*p*TSA) (6.06 g, 31.84 mmol). The reaction mixture was stirred at 53 °C for 16 h, then triethylamine (10 mL) was added and the reaction mixture stirred at ambient temperature for 10 min. The reaction mixture was concentrated under reduced pressure. Gradient flash chromatography (Dichloromethane/methanol, 100:0 → 97:3 → 95:5) afforded the protected alcohol (9.84 g, 89%) as a colorless oil: TLC R_f = 0.50 (5% MeOH/CH₂Cl₂); [α]_D²⁵ -2.6 (*c* 0.935, CHCl₃); IR (neat) 3416 (br, m), 2972 (s), 2939 (s), 2881 (s), 1464 (s), 1355 (s), 1294 (m), 1205 (s), 1172 (s), 1134 (s), 1078 (s), 1055 (s), 991 (s), 959 (s), 916 (s), 764 (s) cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 4.24 (app qn, *J* = 7.2 Hz, 1 H, C₄-H), 4.09 (dd, *J* = 8.0, 6.3

Hz, 1 H, C₅-H), 3.80 (s, 2 H, C₁-H₂), 3.54 (t, *J* = 8.0 Hz, 1 H, C₅-H), 2.30 (s, 1 H, C₁OH), 1.81 (m, 2 H, C₂-H₂), 1.65 (q, *J* = 7.4 Hz, 2 H, CH₂CH₃), 1.62 (q, *J* = 7.4 Hz, 2 H, CH₂CH₃), 0.90 (t, *J* = 7.4 Hz, 3 H, CH₂CH₃), 0.89 (t, *J* = 7.4 Hz, 3 H, CH₂CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 113.0 (C₂), 75.5 (C₄), 70.1 (C₅), 60.8 (C₁), 35.4 (C₂), 29.9 (CH₂CH₃), 29.60 (CH₂CH₃), 8.2 (CH₂CH₃), 7.9 (CH₂CH₃); high resolution mass spectrum (+ESI) *m/z* 197.1154 [(M+Na)⁺; calcd for C₉H₁₈O₃Na: 197.1154].

4(R) (2,2-Diethyl-[1,3]dioxolan-4-yl)-acetaldehyde

To a solution of 2(R)-2-(2,2-diethyl-[1,3]dioxolan-4-yl)-ethanol (4.00 g, 22.96 mmol) and 4 Å molecular sieves (11.50 g) in dichloromethane (200 mL) stirred at 0 °C for 5 min. was added pyridinium chlorochromate (PCC) (9.90 g, 45.92 mmol). The reaction mixture was allowed to warm to ambient temperature and stirred for 1 h. The crude reaction mixture was filtered through a plug of silica, washed with diethyl ether (50 mL) and concentrated under reduced pressure to afford the aldehyde (3.56 g, 90%) as a colorless oil: TLC R_f = 0.60 (5% MeOH/CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃) δ 9.18 (s, 1 H, C₁-H), 4.30 (m, 1 H, C₄-H), 4.15 (dd, *J* = 8.1, 6.1 Hz, 1 H, one of C₅-H₂), 3.72 (dd, *J* = 8.1, 6.8 Hz, 1 H, one of C₅-H₂), 2.78 (dd, *J* = 17.3, 5.2 Hz, 1 H, one of C₂-H₂), 2.68 (dd, *J* = 17.3, 6.7 Hz, 1 H, one of C₂-H₂), 1.68 (q, *J* = 7.5 Hz, 2 H, CH₂CH₃), 1.63 (q, *J* = 7.5 Hz, 2 H, CH₂CH₃), 0.93 (t, *J* = 7.5 Hz, 3 H, CH₂CH₃), 0.90 (t, *J* = 7.5 Hz, 3 H, CH₂CH₃); high resolution mass spectrum (+ESI) *m/z* 195.0997 [(M+Na)⁺; calcd for C₉H₁₆O₃Na: 195.0997].

4(R) 4-(2,2-Diethyl-[1,3]dioxolan-4-yl)-1,1-dibromoprop-1-ene (6).

To a solution of triphenylphosphine (2.47 g, 9.41 mmol) and carbon tetrabromide (1.56 g, 4.70 mmol) in dichloromethane (20 mL) stirred at 0 °C for 5 min. was added a solution of 2(R) (2,2-diethyl-[1,3]dioxolan-4-yl)-acetaldehyde (0.50 g, 2.35 mmol) in dichloromethane (5 mL). The reaction mixture was stirred at 0 °C for 5 min. The reaction mixture was quenched with saturated solution of aqueous K₂CO₃. The layers were separated, and the aqueous phase was extracted with dichloromethane (3 × 50 mL). The combined organic extracts were washed with H₂O (1 × 50 mL), and brine (1 × 50 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 → 98:2 → 96:4 → 94:6) afforded 6 (0.64 g, 82%) as a colorless oil: TLC R_f = 0.56 (10% Et₂O/P.E.); [α]_D²⁵ -1.9 (c 0.365, CHCl₃); IR (neat) 2972 (m), 2937 (m), 2880 (m), 1621 (w), 1463 (m), 1355 (m), 1261 (m), 1228 (m), 1196 (m), 1171 (m), 1077 (s), 1058 (s), 965 (m), 923 (m), 881 (m), 782 (s) cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 6.50 (t, *J* = 7.1 Hz, 1 H, C₂-H), 4.19 (m, 1 H, C₄-

H), 4.06 (dd, $J = 7.9, 6.2$ Hz, 1 H, one of C_5 - H_2), 3.55 (t, $J = 7.7$ Hz, 1 H, one of C_5 - H_2), 2.39 (app t, $J = 6.5$ Hz, 2 H, C_3 - H_2), 1.66 (q, $J = 7.5$ Hz, 2 H, CH_2CH_3), 1.62 (q, $J = 7.5$ Hz, 2 H, CH_2CH_3), 0.92 (t, $J = 7.5$ Hz, 3 H, CH_2CH_3), 0.90 (t, $J = 7.5$ Hz, 3 H, CH_2CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ 134.0 (C_2), 113.3 (C_2), 90.9 (C_1), 74.0 (C_4), 69.2 (C_5), 37.0 (C_3), 29.8 (CH_2CH_3), 29.4 (CH_2CH_3), 8.2 (CH_2CH_3), 7.9 (CH_2CH_3); high resolution mass spectrum (+ESI) m/z [M^+ ; calcd for $C_{10}H_{16}O_2Na$: 350.9394].

4'(R) 4-(2,2'-Diethyl-[1',3']dioxolan-4'-yl)-but-2-ynal (7).

To a solution of 4(*R*) 4-(2,2-diethyl-[1,3]dioxolan-4-yl)-1,1-dibromoprop-1-ene (**6**) (1.50 g, 4.56 mmol) in tetrahydrofuran (100 mL) stirred at -78 °C for 30 min. was added a solution of *n*BuLi (1.6 M in hexane) (7.13 mL, 11.40 mmol). The reaction mixture was stirred at -78 °C for 1 h. To the reaction mixture was added a solution of *N*-formylmorpholine (0.74 g, 6.39 mmol) in tetrahydrofuran (5 mL). The reaction mixture was allowed to warm to ambient temperature over 17 h. The reaction mixture was quenched with saturated solution of aqueous NH_4Cl (100 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (3×100 mL). The combined organic extracts were washed with H_2O (1×100 mL), and brine (1×100 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 $\rightarrow$ 95:5 $\rightarrow$ 90:10 $\rightarrow$ 80:20) afforded **7** (0.62 g, 70%) as a colorless oil: TLC R_f = 0.16 (10 % Et_2O /P.E.); $[\alpha]_D^{25}$ -37.7 (*c* 0.345, $CHCl_3$); IR (neat) 2973 (m), 2939 (m), 2883 (m), 2280 (w), 2203 (m), 1670 (s), 1464 (m), 1387 (m), 1356 (m), 1297 (m), 1273 (m), 1199 (m), 1172 (m), 1136 (s), 1079 (s), 1060 (s), 1042 (s), 965 (m), 918 (s), 828 (s), 768 (m), 678 (m) cm^{-1} ; 1H NMR (600 MHz, $CDCl_3$) δ 9.18 (s, 1 H, C_1 - H), 4.30 (app qn, $J = 6.4$ Hz, 1 H, C_4 - H), 4.15 (dd, $J = 8.2, 6.1$ Hz, 1 H, one of C_5 - H_2), 3.72 (dd, $J = 8.2, 6.7$ Hz, 1 H, one of C_5 - H_2), 2.75 (dd, $J = 17.4, 5.3$ Hz, 1 H, one of C_4 - H_2), 2.68 (dd, $J = 17.4, 6.7$ Hz, 1 H, one of C_4 - H_2), 1.68 (q, $J = 7.5$ Hz, 2 H, CH_2CH_3), 1.63 (q, $J = 7.5$ Hz, 2 H, CH_2CH_3), 0.92 (t, $J = 7.5$ Hz, 3 H, CH_2CH_3), 0.90 (t, $J = 7.5$ Hz, 3 H, CH_2CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ 176.7 (C_1), 114.0 (C_2), 93.7 (C_2), 82.5 (C_3), 73.1 (C_4), 69.1 (C_5), 29.7 (CH_2CH_3), 29.3 (CH_2CH_3), 24.2 (C_4), 8.1 (CH_2CH_3), 7.9 (CH_2CH_3); high resolution mass spectrum (+ESI) m/z 219.0997 [M^+ ; calcd for $C_{11}H_{16}O_3Na$: 219.0997].

4(R) 6-(2,2-Diethyl-[1,3]dioxolane-4-yl)-hexa-1,4-diyn-3-ol

To a solution of 4-(2,2-diethyl-[1,3]dioxolane-4-yl)-but-2-ynal (**7**) (0.43g, 2.04 mmol) in tetrahydrofuran (10 mL) stirred at -78 °C for 30 min. was added a solution of ethynylmagnesium bromide (0.5 M in tetrahydrofuran) (8.15 mL, 4.07 mmol). The reaction mixture was allowed to warm to -30 °C and stirred for 30 min. The reaction

mixture was quenched with saturated solution of aqueous NH_4Cl (10 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (3×10 mL). The combined organic extracts were washed with H_2O (1×10 mL), and brine (1×10 mL), dried over MgSO_4 , filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 $\rightarrow$ 90:10 $\rightarrow$ 80:20 $\rightarrow$ 60:40) afforded the bis-ynol (0.43 g, 95%) as a clear pale yellow oil: TLC R_f = 0.56 (40% $\text{Et}_2\text{O}/\text{P.E.}$); $[\alpha]_D^{25}$ -43.0 (c 1.31, CHCl_3); IR (neat) 3287 (br, m), 2941 (s), 2973 (s), 2883 (m), 2233 (w), 2123 (w), 1463 (s), 1380 (m), 1356 (m), 1297 (s), 1199 (s), 1171 (s), 1137 (s), 1078 (s), 1023 (s), 965 (m), 915 (s), 808 (m), 767 (m), 733 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 5.09 (dd, J = 7.4, 2.3 Hz, 1 H, $\text{C}_3\text{-H}$), 4.24 (app qn, J = 7.0 Hz, 1 H, $\text{C}_4\text{-H}$), 4.13 (dd, J = 8.1, 6.1 Hz, 1 H, one of $\text{C}_5\text{-H}_2$), 3.73 (app t, J = 7.5 Hz, 1 H, one of $\text{C}_5\text{-H}_2$), 2.62 (ddd, J = 16.7, 4.8, 2.0 Hz, 1 H, one of $\text{C}_6\text{-H}_2$), 2.54 (d, J = 2.3 Hz, 1 H, $\text{C}_1\text{-H}$), 2.50 (ddd, J = 16.7, 7.4, 2.1 Hz, 1 H, one of $\text{C}_6\text{-H}_2$), 2.33 (d, J = 7.4 Hz, 1 H, C_3OH), 1.67 (q, J = 7.5 Hz, 2 H, CH_2CH_3), 1.62 (q, J = 7.5 Hz, 2 H, CH_2CH_3), 0.92 (t, J = 7.5 Hz, 3 H, CH_2CH_3), 0.90 (t, J = 7.5 Hz, 3 H, CH_2CH_3); ^{13}C NMR (100 MHz, CDCl_3) δ 113.7 (C_2), 81.13 (C_4), 81.11 (C'_4), 81.04 (C_5), 78.9 (C_2), 73.8 (C_4), 72.5 (C_1), 69.2 (C_5), 69.2 (C'_5), 52.1 (C_3), 29.8 (CH_2CH_3), 29.5 (CH_2CH_3), 23.6 (C_6), 23.6 (C'_6), 8.1 (CH_2CH_3), 8.0 (CH_2CH_3); high resolution mass spectrum (+ESI) m/z 245.1154 [$(\text{M}+\text{Na})^+$; calcd for $\text{C}_{13}\text{H}_{18}\text{O}_3\text{Na}$: 245.1154].

4 (R) 6-(2,2-Diethyl-[1,3]dioxolane-4-yl)-hexa-1,4-diyn-3-one (8).

To a solution of 6-(2,2-diethyl-[1,3]dioxolane-4-yl)-hexa-1,4-diyn-3-ol (0.85 g, 3.84 mmol) in dichloromethane (20 mL) stirred at 0 °C for 30 min. was added Dess-Martin periodinane (2.45 g, 5.77 mmol). The reaction mixture was allowed to warm to ambient temperature and stirred for 30 min. The reaction mixture was quenched with a 1:1 solution of saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ and saturated aqueous NaHCO_3 (10 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (3×20 mL). The combined organic extracts were washed with H_2O (1×20 mL), and brine (1×20 mL), dried over MgSO_4 , filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 $\rightarrow$ 90:10 $\rightarrow$ 80:20 $\rightarrow$ 60:40) afforded **8** (0.82 g, 97%) as a clear yellow oil: TLC R_f = 0.61 (50% $\text{Et}_2\text{O}/\text{P.E.}$); $[\alpha]_D^{25}$ -18.0 (c 0.05, CHCl_3); IR (neat) 3250 (br, m), 2975 (s), 2940 (s), 2883 (s), 2225 (s), 2097 (s), 1633 (s), 1463 (s), 1379 (m), 1356 (m), 1273 (s), 1208 (s), 1172 (s), 1131 (s), 1079 (s), 1041 (s), 955 (s), 916 (s), 726 (s) cm^{-1} ; ^1H NMR (600 MHz, CDCl_3) δ 4.30 (m, 1 H, $\text{C}_4\text{-H}$), 4.15 (dd, J = 8.1, 6.1 Hz, 1 H, one of $\text{C}_5\text{-H}_2$), 3.74 (dd, J = 8.1, 6.9 Hz, 1 H, one of $\text{C}_5\text{-H}_2$), 3.29 (s, 1 H, $\text{C}_1\text{-H}$), 2.76 (dd, J = 17.4, 4.9 Hz, 1 H, one of $\text{C}_6\text{-H}_2$), 2.70 (dd, J = 17.4, 6.7 Hz, 1 H, one of $\text{C}_6\text{-H}_2$), 1.68 (q, J = 7.5 Hz, 2 H, CH_2CH_3), 1.62 (q, J = 7.5 Hz, 2 H, CH_2CH_3), 0.91 (t, J = 7.5 Hz, 3 H, CH_2CH_3), 0.90 (t, J = 7.5 Hz, 3 H, CH_2CH_3); ^{13}C NMR (150 MHz, CDCl_3) δ 159.9 (C_3), 114.0 (C_2), 91.3 (C_5), 82.8 (C_4), 82.1 (C_2), 78.6 (C_1), 73.0 (C_4), 69.0 (C_5), 29.7 (CH_2CH_3), 29.4 (CH_2CH_3), 24.1 (C_6), 8.1 (CH_2CH_3),

8.0 (CH₂CH₃); high resolution mass spectrum (+ESI) m/z 243.0997 [(M+Na)⁺; calcd for C₁₃H₁₆O₃Na: 243.0997]; elemental analysis C, 70.74%; H, 7.44%.

4 (R) 1-([1,3]Dithian-2-yl)-5-([1,3]dithian-2-yl)-6(2,2-diethyl-[1,3]dioxolane-4-yl)-hexa-3-one (9).

To a solution of 6-(2,2-diethyl-[1,3]dioxolane-4-yl)-hexa-1,4-dien-3-one (**8**) (400 mg, 1.82 mmol) and propane-1,3-dithiol (433 mg, 4.00 mmol) in dichloromethane (16 mL) and methanol (16 mL) stirred at -10 °C for 30 min. was added sodium methoxide (216 mg, 4.00 mmol). The reaction mixture was allowed to warm to ambient temperature over 17 h. The reaction mixture was quenched with saturated aqueous NH₄Cl solution (20 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (3 × 20 mL). The combined organic extracts were washed with H₂O (1 × 20 mL), and brine (1 × 20 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 → 90:10 → 80:20 → 70:30 → 60:40) afforded **9** (0.68 g, 86%) as a clear pale yellow oil: TLC R_f = 0.40 (50% Et₂O/P.E.); $[\alpha]_D^{25}$ +2.6 (c 1.035, CHCl₃); IR (neat) 2967 (s), 2932 (s), 2359 (w), 1723 (s), 1462 (s), 1422 (s), 1352 (s), 1276 (s), 1241 (m), 1194 (s), 1171 (s), 1077 (s), 912 (s), 873 (m), 765 (m), 658 (m) cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 4.49 (t, J = 6.5 Hz, 1 H, C₁-H), 4.38 (m, 1 H, C₄-H), 4.10 (dd, J = 7.7, 6.1 Hz, 1 H, one of C₅-H₂), 3.48 (t, J = 8.2 Hz, 1 H, one of C₅-H₂), 3.27 (d, J = 16.5 Hz, 1 H, one of C₄-H₂), 3.13 (d, J = 16.5 Hz, 1 H, one of C₄-H₂), 2.86 (m, 10 H, both of SCH₂CH₂CH₂S and C₂-H₂), 2.54 (dd, J = 14.9, 8.1 Hz, 1 H, one of C₆-H₂), 2.29 (dd, J = 14.9, 2.7 Hz, 1 H, one of C₆-H₂), 2.08 (m, 1 H, one of SCH₂CH₂CH₂S), 1.97 (app q, J = 6.0 Hz, 2 H, SCH₂CH₂CH₂S), 1.85 (m, 1 H, one of SCH₂CH₂CH₂S), 1.59 (m, 4 H, both of CH₂CH₃), 0.88 (t, J = 7.5 Hz, 3 H, CH₂CH₃), 0.86 (t, J = 7.5 Hz, 3 H, CH₂CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 201.4 (C₃), 113.2 (C₂'), 73.0 (C₄'), 70.4 (C₅'), 51.0 (C₄), 49.2 (C₂), 48.6 (C₅), 41.0 (C₆), 40.9 (C₁), 30.3 (SCH₂CH₂CH₂S), 30.2 (SCH₂CH₂CH₂S), 30.0 (CH₂CH₃), 30.0 (CH₂CH₃), 26.4 (SCH₂CH₂CH₂S), 26.4 (SCH₂CH₂CH₂S), 25.3 (SCH₂CH₂CH₂S), 24.8 (SCH₂CH₂CH₂S), 8.3 (CH₂CH₃), 7.9 (CH₂CH₃); high resolution mass spectrum (+ESI) m/z 459.1132 [(M+Na)⁺; calcd for C₁₉H₃₂O₃S₄Na: 459.1132]; elemental analysis C, 52.40%; H, 7.38%.

Dithiane (10)

To a solution of 4 (*R*) 1-([1,3]dithian-2-yl)-5-([1,3]dithian-2-yl)-6(2,2-diethyl-1,3)dioxolane-4-yl)-hexa-3-one (**9**). (50 mg, 0.11 mmol) in tetrahydrofuran (0.5 mL), trimethylorthoformate (0.5 mL) and methanol (5 mL) was added 10-camphorsulfonic acid (40 mg, 0.17 mmol). The reaction mixture was heated to 45 °C for 4 h. The reaction mixture was quenched with saturated aqueous NaHCO₃ solution (5 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (3 × 5 mL). The combined organic extracts were washed with H₂O (1 × 5 mL), and brine (1 × 5 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 → 90:10 → 80:20 → 70:30 → 60:40 → 50:50 → 40:60) afforded **10** (28.8 mg, 70%, or 83% by recovered starting material) an inseparable mixture of the desired methyl hemiketal and the enol ether as a white foam, and recovered **9** (8.0 mg) as a clear pale yellow oil. In order to ascertain the ratio of enol ether to the methyl hemiketal, the mixture of products was silylated, and separated.

¹H NMR (600 MHz, CDCl₃) δ 6.96 (s), 4.99 (s), 4.80 (s), 4.75 (s), 4.25 (m), 4.12 (dd, *J* = 4.1, 7.5 Hz), 4.03 (m), 3.85 (m), 3.72 (m), 3.59 (m), 3.32 (m), 3.19 (s), 3.08 (dt, *J* = 2.6, 14.1 Hz), 2.98 (dt, *J* = 1.8, 14.1 Hz), 2.93 (d, *J* = 1.9 Hz), 2.90 (d, *J* = 6.1 Hz), 2.86 (tdd, *J* = 0.9, 3.9, 10.5 Hz), 2.80 (dt, *J* = 3.3, 10.5 Hz), 2.67 (m), 2.56 (d, *J* = 13.8 Hz), 2.53 (d, *J* = 6.7 Hz), 2.50 (t, *J* = 7.6 Hz), 2.47 (d, *J* = 7.6 Hz), 2.41 (d, *J* = 14.2 Hz), 2.26 (s), 2.10 (m), 1.96 (dd, *J* = 7.7, 15.2 Hz), 1.84 (m), 1.65 (s), 1.42 (s), 1.24 (s); ¹³C NMR (150 MHz, CDCl₃) δ 152.2, 125.5, 102.5, 99.6, 74.5, 68.6, 65.2, 64.6, 53.4, 47.7, 46.6, 44.9, 42.7, 41.7, 39.9, 37.3, 31.2, 30.8, 30.4, 30.3, 29.6, 27.3, 27.0, 26.5, 26.3, 25.7, 25.3, 25.2, 24.5; high resolution mass spectrum (+ESI) *m/z* 373.0400 [(M+Na)⁺; calcd for C₁₄H₂₂O₂S₄Na: 373.0400] *m/z* 405.0663 [(M+Na)⁺; calcd for C₁₅H₂₆O₃S₄Na: 405.0662].

Silylated Dithiane

To a solution of **10** (28.8 mg, as a mixture of pyrans) in tetrahydrofuran (2.0 mL), was added imidazole (14 mg, 0.21 mmol) and TBSCl (16 mg, 0.10 mg). The reaction mixture was stirred at ambient temperature for 16 h. The reaction mixture was poured through a fritted tube to remove excess salt and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 → 99:1 → 98:2 → 97:3 → 96:4 → 95:5 → 94:6 → 92:8 → 90:10) afforded TBS protected enol ether (26.2 mg) and TBS protected methyl hemiketal (10.3 mg) as yellow oils.

TBS protected enol ether

TLC R_f = 0.24 (10% Et₂O/P.E.); ¹H NMR (600 MHz, CDCl₃) δ 4.78 (s, 1 H, C₄-H), 4.25 (t, *J* = 7.4 Hz, 1 H, C₁-H), 4.17 (m, 1 H, C₇-H), 3.81 (dd, *J* = 4.7, 10.6 Hz, 1 H, one of C₈-

H_2), 3.75 (dd, $J = 4.8, 10.6$ Hz, 1 H, one of C_8-H_2), 2.98 (m, 2 H, $SCH_2CH_2CH_2S$), 2.81 (m, 5 H, $SCH_2CH_2CH_2S$), 2.69 (d, $J = 13.7$ Hz, 1 H, one of C_6-H_2), 2.64 (d, $J = 13.7$ Hz, 1 H, one of C_6-H_2), 2.49 (dd, $J = 6.9, 13.9$ Hz, 1 H, one of C_2-H_2), 2.43 (dd, $J = 8.0, 13.9$ Hz, 1 H, one of C_2-H_2), 2.07 (m, 2 H, $SCH_2CH_2CH_2S$), 1.97 (app t, $J = 12.4$ Hz, 1 H, one of $SCH_2CH_2CH_2S$), 1.85 (m, 2 H, $SCH_2CH_2CH_2S$), 0.91 (s, 9 H, $OSi(CH_3)_2C(CH_3)_3$), 0.09 (s, 6 H, $OSi(CH_3)_2C(CH_3)_3$); ^{13}C NMR (150 MHz, $CDCl_3$) δ 152.3 (C_3), 102.3 (C_4), 74.5 (C_7), 64.9 (C_8), 45.2 (C_5), 44.0 (C_1), 40.0 (C_2), 37.9 (C_6), 30.1 ($SCH_2CH_2CH_2S$), 30.0 ($SCH_2CH_2CH_2S$), 27.4 ($SCH_2CH_2CH_2S$), 26.9 ($SCH_2CH_2CH_2S$), 25.9 ($OSi(CH_3)_2C(CH_3)_3$), 25.8 ($SCH_2CH_2CH_2S$), 24.6 ($SCH_2CH_2CH_2S$), -3.6 ($OSi(CH_3)_2C(CH_3)_3$), -5.3 ($OSi(CH_3)_2C(CH_3)_3$).

TBS protected methyl hemiketal

TLC $R_f = 0.12$ (10% $Et_2O/P.E.$); 1H NMR (600 MHz, $CDCl_3$) δ 4.12 (dd, $J = 4.5, 6.7$ Hz, 1 H, C_1-H), 3.98 (m, 1 H, C_7-H), 3.71 (dd, $J = 5.6, 10.5$ Hz, 1 H, one of C_8-H_2), 3.60 (dd, $J = 5.3, 10.5$ Hz, 1 H, one of C_8-H_2), 3.19 (s, 3 H, C_3OCH_3), 3.09 (m, 1H, $SCH_2CH_2CH_2S$), 2.91 (m, 3 H, $SCH_2CH_2CH_2S$), 2.77 (m, 2 H, $SCH_2CH_2CH_2S$), 2.70 (m, 1 H, $SCH_2CH_2CH_2S$), 2.57 (app d, $J = 13.7$ Hz, 2 H, C_4-H_2), 2.13 (dd, $J = 4.3, 15.5$ Hz, 1 H, one of C_2-H_2), 2.06 (m, 1 H, $SCH_2CH_2CH_2S$), 1.84 (m, 3 H, $SCH_2CH_2CH_2S$ and one of C_2-H_2), 1.63 (m, 2 H, $SCH_2CH_2CH_2S$), 0.90 (s, 9 H, $OSi(CH_3)_2C(CH_3)_3$), 0.07 (s, 6 H, $OSi(CH_3)_2C(CH_3)_3$); ^{13}C NMR (150 MHz, $CDCl_3$) δ 99.5 (C_3), 68.7 (C_7), 65.7 (C_8), 47.6 (C_3OCH_3), 46.8 (C_5), 45.7 (C_1), 42.9 (C_2), 38.2 (C_4), 31.2 ($SCH_2CH_2CH_2S$), 30.9 ($SCH_2CH_2CH_2S$), 30.3 (C_6), 29.7 ($SCH_2CH_2CH_2S$), 26.5 ($SCH_2CH_2CH_2S$), 25.9 ($OSi(CH_3)_2C(CH_3)_3$), 25.3 ($SCH_2CH_2CH_2S$), 18.3 ($SCH_2CH_2CH_2S$), 1.0 ($OSi(CH_3)_2C(CH_3)_3$), -5.3 ($OSi(CH_3)_2C(CH_3)_3$).

2(R), 3(S), 4(R), 2,4-Dimethyl-hex-5-ene-1,3-diol (11).

A solution of tetrabutylammonium fluoride (TBAF) (1.0 M in THF) (39.20 mL, 39.20 mmol) was added dropwise to a solution of 2 (*R*), 3 (*S*), 1-(*tert*-butyldiphenylsilyloxy)-2,4-dimethyl-3-hydroxy-5-hexene (10.00 g, 26.14 mmol) in anhydrous tetrahydrofuran (250 mL). The colorless mixture was then stirred at ambient temperature for 1 h at which time a solution of TBAF (1.0 M in THF) (13.07 mL, 13.07 mmol) was added and the reaction mixture was stirred at ambient temperature for 20 min. The reaction was quenched with saturated aqueous NH_4Cl solution (100 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (3×100 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/ diethyl ether, 100:0 $\rightarrow$ 75:25

→ 50:50 → 40:60 → 25:75) afforded **11** (3.60 g, 95%) as a clear pale yellow oil: TLC R_f = 0.12 (50% Et₂O/P.E.); $[\alpha]_D^{25}$ +11.5 (*c*1.05, CHCl₃); IR (neat) 3339 (br, s), 2965 (s), 2878 (s), 1640 (s), 1456 (s), 1420 (s), 1377 (s), 1069 (s), 1027 (s), 996 (s), 969 (s), 911 (s), 859 (w), 733 (s), 679 (s) cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.85 (ddd, *J* = 17.2, 10.8, 6.5 Hz, 1 H, C₅-*H*), 5.14 (s, 1 H, one of C₆-*H*₂), 5.09 (d, *J* = 1.3 Hz, 1 H, one of C₆-*H*₂), 3.75 (dd, *J* = 10.8, 3.5 Hz, 1 H, one of C₁-*H*₂), 3.64 (dd, *J* = 10.8, 7.1 Hz, 1 H, one of C₁-*H*₂), 3.48 (dd, *J* = 7.9, 3.9 Hz, 1 H, C₃-*H*), 2.45 (m, 1 H, C₄-*H*), 1.85 (m, 1 H, C₂-*H*), 1.03 (d, *J* = 6.9 Hz, 3 H, C₄CH₃), 0.90 (d, *J* = 7.0 Hz, 3 H, C₂CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 141.5 (C₅), 115.3 (C₆), 79.6 (C₃), 67.9 (C₁), 40.1 (C₄), 36.9 (C₂), 13.8 (C₂CH₃), 11.7 (C₄CH₃); high resolution mass spectrum (+ESI) *m/z* 167.1048 [(M+Na)⁺; calcd for C₈H₁₆O₂Na: 167.1048].

Paramethoxybenzylidene acetal (**17**)

Under argon, a solution of 2(*R*), 3(*S*), 4(*R*), 2,4-dimethyl-hex-5-ene-1,3-diol (**11**) (3.46 g, 23.99 mmol) and *p*-anisaldehyde dimethyl acetal (21.86 g, 119.96 mmol) in anhydrous chloroform (200 mL) was treated with *p*-TsOH (456 mg, 2.40 mmol). The reaction mixture was stirred at ambient temperature for 1 h 25 min. The pale pink reaction mixture was quenched with saturated aqueous NaHCO₃ solution (100 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (3 × 100 mL). The combined organic extracts were dried over MgSO₄, filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 → 90:10 → 80:20 → 70:30 → 60:40) afforded the paramethoxybenzylidene acetal (5.73 g, 91%) as a clear pale yellow oil: TLC R_f = 0.87 (50% Et₂O/P.E.); $[\alpha]_D^{25}$ -67.2 (*c*1.025, CHCl₃); IR (neat) 2934 (s), 2965 (s), 2836 (s), 1615 (s), 1588 (w), 1517 (s), 1460 (s), 1419 (w), 1391 (s), 1370 (s), 1302 (s), 1247 (s), 1170 (s), 1147 (s), 1119 (s), 1077 (s), 1032 (s), 981 (s), 958 (s), 912 (s), 825 (s), 782 (s), 666 (s) cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 7.42 (d, *J* = 8.7 Hz, 2 H, Ar-*H*₂, H_a), 6.89 (d, *J* = 8.7 Hz, 2 H, Ar-*H*₂, H_b), 6.03 (ddd, *J* = 17.2, 10.3, 7.6 Hz, 1 H, C₅-*H*), 5.44 (s, 1H, CHAr), 5.08 (d, *J* = 17.2 Hz, 1 H, C₆-*H*₂, H_c), 5.01 (d, *J* = 10.3 Hz, 1 H, C₆-*H*₂, H_d), 4.10 (dd, *J* = 11.0, 4.7 Hz, 1 H, one of C₁-*H*₂), 3.80 (s, 3H, ArOCH₃), 3.50 (t, *J* = 11.0 Hz, 1 H, one of C₁-*H*₂), 3.45 (dd, *J* = 10.0, 2.4 Hz, 1 H, C₃-*H*), 2.50 (m, 1 H, C₄-*H*), 2.04 (m, 1 H, C₂-*H*), 1.11 (d, *J* = 6.9 Hz, 3 H, C₄CH₃), 0.80 (d, *J* = 6.7 Hz, 3 H, C₂CH₃); ¹³C NMR (150 MHz, CDCl₃) δ 159.8 (Ar, C-OCH₃), 142.4 (C₅), 131.5 (Ar), 127.3 (Ar, C-H_a), 113.6 (C₆), 113.5 (Ar, C-H_b), 100.9 (CHAr), 86.0 (C₃), 73.1 (C₁), 55.3 (ArOCH₃), 39.0 (C₄), 30.9 (C₂), 13.2 (C₄CH₃), 12.2 (C₂CH₃); high resolution mass spectrum (+ESI) *m/z* 285.1467 [(M+Na)⁺; calcd for C₁₆H₂₂O₃Na: 285.1467].

2(*R*), 3(*S*), 4(*R*), 3-(4'-Methoxy-benzoyloxy)-2,4-dimethyl-hex-5-en-1-ol

Under argon, a solution of **17** (2.00 g, 7.62 mmol), in dichloromethane (100 mL) at -10°C was treated with a solution of DIBAL-H (1 M in CH_2Cl_2) (19.06 mL, 19.06 mmol). The reaction mixture was stirred at -10°C for 2 h. The reaction mixture was quenched with a 1:1 solution of methanol and toluene (20 mL) and poured into saturated Rochelle's salt (sodium potassium tartrate) solution and stirred for 1 h. The layers were separated, and the aqueous phase was extracted with diethyl ether (4×100 mL). The combined organic extracts were washed with 1 M HCl (1×100 mL), H_2O (1×100 mL), and brine (1×100 mL), dried over MgSO_4 , filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 $\rightarrow$ 90:10 $\rightarrow$ 80:20 $\rightarrow$ 70:30 $\rightarrow$ 60:40 $\rightarrow$ 50:50 $\rightarrow$ 40:60) afforded the alcohol (4.81 g, 87%) as a clear pale yellow oil: TLC R_f = 0.30 (50% $\text{Et}_2\text{O}/\text{P.E.}$); $[\alpha]_D^{25} +34.1$ (c 1.055, CHCl_3); IR (neat) 3426 (m, br), 2964 (s), 2874 (s), 1638 (m), 1613 (s), 1586 (m), 1513 (s), 1456 (s), 1420 (m), 1347 (m), 1301 (s), 1246 (s), 1173 (s), 1033 (s), 951 (s), 913 (s), 821 (s), 757 (s), 682 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.26 (d, J = 8.6 Hz, 2 H, Ar- H_2 , H_a), 6.87 (d, J = 8.6 Hz, 2 H, Ar- H_2 , H_b), 5.90 (ddd, J = 17.3, 10.3, 7.4 Hz, 1 H, $\text{C}_5\text{-H}$), 5.09 (d, J = 17.3 Hz, 1 H, $\text{C}_6\text{-H}_2$, H_c), 5.04 (d, J = 10.3 Hz, 1 H, $\text{C}_6\text{-H}_2$, H_d), 4.60 (d, J = 10.6 Hz, 1 H, one of CH_2Ar), 4.47 (d, J = 10.6 Hz, 1 H, one of CH_2Ar), 3.80 (s, 3 H, ArOCH_3), 3.70 (m, 1 H, one of $\text{C}_1\text{-H}_2$), 3.58 (m, 1 H, one of $\text{C}_1\text{-H}_2$), 3.30 (dd, J = 5.7, 5.7 Hz, 1 H, $\text{C}_3\text{-H}$), 2.80 (dd, J = 5.5 Hz, 5.5 Hz, 1 H, C_1OH), 2.53 (m, 1 H, $\text{C}_4\text{-H}$), 1.90 (m, 1 H, $\text{C}_2\text{-H}$), 1.11 (d, J = 6.8 Hz, 3 H, C_4CH_3), 1.00 (d, J = 7.1 Hz, 3 H, C_2CH_3); ^{13}C NMR (100 MHz, CDCl_3) δ 159.3 (Ar, C-OCH_3), 142.0 (C_5), 130.3 (Ar), 129.5 (Ar, C-H_a), 114.3 (C_6), 113.8 (Ar, C-H_b), 88.3 (C_3), 74.7 (CH_2Ar), 66.0 (C_1), 55.2 (ArOCH_3), 40.8 (C_4), 37.2 (C_2), 15.5 (C_2CH_3), 14.6 (C_4CH_3); high resolution mass spectrum (+ESI) m/z 287.1623 [(M+Na) $^+$; calcd for $\text{C}_{16}\text{H}_{24}\text{O}_3\text{Na}$: 287.1623].

2(R), 3(S), 4(R), 3-(4'-Methoxy-benzyloxy)-2,4-dimethyl-hex-5-enal

Under argon, a solution of 2(R), 3(S), 4(R), 3-(4-methoxy-benzyloxy)-2,4-dimethyl-hex-5-en-1-ol (1.40 g, 5.28 mmol), in dichloromethane (50 mL) at 0°C was treated with Dess-Martin Periodinane (3.36 g, 7.92 mmol). The reaction mixture was stirred at ambient temperature for 2 h. The reaction mixture was quenched with a 1:1 solution of saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ and saturated aqueous NaHCO_3 (10 mL). The layers were

separated, and the aqueous phase was extracted with diethyl ether (3×50 mL). The combined organic extracts were washed with H_2O (1×50 mL), and brine (1×50 mL), dried over MgSO_4 , filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 $\rightarrow$ 90:10 $\rightarrow$ 80:20) afforded the aldehyde (1.30 g, 94%) as a clear pale yellow oil: TLC $R_f = 0.77$ (50% $\text{Et}_2\text{O}/\text{P.E.}$); $[\alpha]_D^{25} +39.9$ (c 1.04, CHCl_3); IR (neat) 2975 (s), 2936 (s), 2875 (s), 2164 (w), 1721 (s), 1639 (m), 1612 (s), 1586 (m), 1513 (s), 1457 (s), 1421 (m), 1394 (m), 1370 (m), 1346 (m), 1302 (s), 1246 (s), 1173 (s), 1033 (s), 1000 (s), 951 (s), 917 (s), 820 (s), 756 (s), 683 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 9.73 (d, $J = 1.9$ Hz, 1 H, $\text{C}_1\text{-H}$), 7.24 (d, $J = 8.5$ Hz, 2 H, Ar-H_2 , H_a), 6.87 (d, $J = 8.5$ Hz, 2 H, Ar-H_2 , H_b), 5.77 (ddd, $J = 17.7, 10.7, 7.9$ Hz, 1 H, $\text{C}_5\text{-H}$), 5.11 (d, $J = 17.7$ Hz, 1 H, $\text{C}_6\text{-H}_2$, H_c), 5.08 (d, $J = 10.7$ Hz, 1 H, $\text{C}_6\text{-H}_2$, H_d), 4.54 (d, $J = 10.8$ Hz, 1 H, one of CH_2Ar), 4.48 (d, $J = 10.8$ Hz, 1 H, one of CH_2Ar), 3.80 (s, 3 H, ArOCH_3), 3.54 (t, $J = 6.1$ Hz, 1 H, $\text{C}_3\text{-H}$), 2.69 (m, 1 H, $\text{C}_2\text{-H}$), 2.54 (m, 1 H, $\text{C}_4\text{-H}$), 1.13 (d, $J = 7.1$ Hz, 3 H, C_2CH_3), 1.11 (d, $J = 6.8$ Hz, 3 H, C_4CH_3); ^{13}C NMR (100 MHz, CDCl_3) δ 204.4 (C_1), 159.2 (Ar, C-OCH_3), 140.7 (C_5), 130.2 (Ar), 129.3 (Ar, C-H_a), 115.8 (C_6), 113.7 (Ar, C-H_b), 84.2 (C_3), 73.4 (CH_2Ar), 55.2 (ArOCH_3), 48.6 (C_2), 40.7 (C_4), 15.5 (C_4CH_3), 11.1 (C_2CH_3); high resolution mass spectrum (+ESI) m/z 285.1467 [$(\text{M}+\text{Na})^+$; calcd for $\text{C}_{16}\text{H}_{22}\text{O}_3\text{Na}$: 285.1467]; elemental analysis C, 72.97%; H, 8.45%.

1,1-Dibromo-3,5-dimethyl-4-(4'-Methoxy-benzyloxy)-hept-1,6-diene (12).

To a solution of triphenylphosphine (3.99 g, 15.20 mmol) and carbon tetrabromide (2.52 g, 7.60 mmol) in dichloromethane (50 mL) stirred at 0°C for 5 min. was added a solution of 2(*R*), 3(*S*), 4(*R*), 3-(4-methoxy-benzyloxy)-2,4-dimethyl-hex-5-enal (1.00 g, 3.80 mmol) in dichloromethane (10 mL). The reaction mixture was stirred at 0°C for 1 h. The reaction mixture was quenched with saturated solution of aqueous K_2CO_3 . The layers were separated, and the aqueous phase was extracted with dichloromethane (3×50 mL). The combined organic extracts were washed with H_2O (1×50 mL), and brine (1×50 mL), dried over MgSO_4 , filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 $\rightarrow$ 98:2 $\rightarrow$ 96:4 $\rightarrow$ 94:6) afforded **12** (1.52 g, 87%) as a clear pale yellow oil: TLC $R_f = 0.70$ (10% $\text{Et}_2\text{O}/\text{P.E.}$); $[\alpha]_D^{25} -38.7$ (c 1.05, CHCl_3); IR (neat) 2963 (s), 2930 (s), 2871 (s), 2835 (s), 2064 (w), 1612 (s), 1586 (s), 1513 (s), 1455 (s), 1420 (m), 1396 (m), 1367 (m), 1349 (s), 1302 (s), 1247 (s), 1172 (s), 1036 (s), 995 (s), 956 (s), 916 (s), 821 (s), 789 (s), 757 (s), 682 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.28 (d, $J = 8.6$ Hz, 2 H, Ar-H_2 , H_a), 6.90 (d, $J = 8.6$ Hz, 2 H, Ar-H_2 , H_b), 6.51 (d, $J = 9.5$ Hz, 1 H, $\text{C}_2\text{-H}$), 5.72 (ddd, $J = 16.9, 9.0, 8.2$ Hz, 1 H, $\text{C}_6\text{-H}$), 5.07 (d, $J = 16.9$ Hz, 1 H, $\text{C}_7\text{-H}_2$, H_c), 5.04 (d, $J = 9.0$ Hz, 1 H, $\text{C}_7\text{-H}_2$, H_d), 4.57 (d, $J = 10.7$ Hz, 1 H, one of CH_2Ar), 4.50 (d, $J = 10.7$ Hz, 1 H, one of CH_2Ar), 3.82 (s, 3 H,

ArOCH₃), 3.14 (dd, $J = 7.9, 2.8$ Hz, 1 H, C₄-H), 2.74 (m, 1 H, C₃-H), 2.36 (m, 1 H, C₅-H), 1.10 (d, $J = 6.2$ Hz, 3 H, C₃CH₃), 1.08 (d, $J = 6.5$ Hz, 3 H, C₅CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 159.2 (Ar, C-OCH₃), 140.6 (C₂), 140.6 (C₆), 130.6 (Ar), 129.4 (Ar-H₂, C-H_a), 115.1 (C₇), 113.7 (Ar-H₂, C-H_b), 88.0 (C₁), 86.0 (C₄), 74.6 (CH₂Ar), 55.3 (ArOCH₃), 42.1 (C₅), 41.4 (C₃), 16.8 (C₅CH₃), 16.6 (C₃CH₃); high resolution mass spectrum (+ESI) m/z 438.9884 [(M+Na)⁺; calcd for C₁₇H₂₂O₂Br₂Na: 438.9884]; elemental analysis C, 49.00%; H, 5.22%.

5-(4'-Methoxy-benzyloxy)-4,6-dimethyl-oct-7-en-2-ynal (**13**).

To a solution of 1,1-dibromo-3,5-dimethyl-4-(4'-Methoxy-benzyloxy)-hept-1,6-diene (**12**) (0.80 g, 1.91 mmol) in tetrahydrofuran (50 mL) stirred at -78 °C for 30 min. was added a solution of *n*BuLi (1.6 M in hexane) (2.99 mL, 4.78 mmol). The reaction mixture was stirred at -78 °C for 1 h. To the reaction mixture was added a solution of *N*-formylmorpholine (0.31 g, 0.27 mmol) in tetrahydrofuran (5 mL). The reaction mixture was allowed to warm to ambient temperature over 3 h. The reaction mixture was quenched with saturated solution of aqueous NH₄Cl (50 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (3 × 50 mL). The combined organic extracts were washed with H₂O (1 × 50 mL), and brine (1 × 50 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 → 95:5 → 90:10 → 88:12 → 84:16) afforded **13** (0.40 g, 73%) as a clear pale yellow oil: TLC R_f = 0.27 (10% Et₂O/P.E.); [α]_D²⁵ -19.5 (*c* 1.025, CHCl₃); IR (neat) 2976 (s), 2935 (s), 2875 (s), 2202 (s), 1662 (s), 1613 (s), 1586 (s), 1513 (s), 1457 (s), 1421 (s), 1389 (s), 1342 (s), 1302 (s), 1246 (s), 1172 (s), 1087 (s), 1062 (s), 1033 (s), 998 (s), 945 (s), 918 (s), 848 (s), 820 (s), 750 (s), 682 (s) cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.18 (s, 1 H, C₁-H), 7.29 (d, $J = 8.6$ Hz, 2 H, Ar-H₂, H_a), 6.88 (d, $J = 8.6$ Hz, 2 H, Ar-H₂, H_b), 5.77 (ddd, $J = 17.1, 10.2, 8.4$ Hz, 1 H, C₇-H), 5.15 (d, $J = 17.1$ Hz, 1 H, C₈-H₂, H_c), 5.05 (dd, $J = 10.2, 0.8$ Hz, 1 H, C₈-H₂, H_d), 4.59 (s, 2 H, CH₂Ar), 3.81 (s, 3 H, ArOCH₃), 3.21 (dd, $J = 7.4, 4.4$ Hz, 1 H, C₅-H), 2.98 (m, 1 H, C₄-H), 2.58 (m, 1 H, C₆-H), 1.29 (d, $J = 7.1$ Hz, 3 H, C₄CH₃), 1.11 (d, $J = 6.7$ Hz, 3 H, C₆CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 177.3 (C₁), 159.3 (Ar, C-OCH₃), 140.7 (C₇), 130.2 (Ar), 129.5 (Ar, C-H_b), 115.6 (C₈), 113.8 (Ar, C-H_a), 100.7 (C₃), 84.8 (C₅), 83.0 (C₂), 74.7 (CH₂Ar), 55.3 (ArOCH₃), 42.0 (C₆), 30.7 (C₄), 17.2 (C₄CH₃), 16.1 (C₆CH₃); high resolution mass spectrum (+ESI) m/z 309.1467 [(M+Na)⁺; calcd for C₁₈H₂₂O₃Na: 309.1467]; elemental analysis C, 75.46%; H, 7.74%.

7-(4'-Methoxy-benzyloxy)-6,8-dimethyl-dec-9-ene-1,4-diyn-3-ol

To a solution of 5-(4'-methoxy-benzyloxy)-4,6-dimethyl-oct-7-en-2-ynal (**13**) (262 mg, 0.91 mmol) in tetrahydrofuran (10 mL) stirred at $-78\text{ }^{\circ}\text{C}$ for 30 min. was added a solution of ethynylmagnesium bromide (0.5 M in tetrahydrofuran) (3.65 mL, 1.83 mmol). The reaction mixture was allowed to warm to $-30\text{ }^{\circ}\text{C}$ and stirred for 30 min. The reaction mixture was quenched with saturated solution of aqueous NH_4Cl (10 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether ($3 \times 10\text{ mL}$). The combined organic extracts were washed with H_2O ($1 \times 10\text{ mL}$), and brine ($1 \times 10\text{ mL}$), dried over MgSO_4 , filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 $\rightarrow$ 90:10 $\rightarrow$ 80:20 $\rightarrow$ 70:30) afforded the bis-ynol (230 mg, 80%) as a clear pale yellow oil: TLC $R_f = 0.08$ (10% $\text{Et}_2\text{O}/\text{P.E.}$); IR (neat) 3290 (m, br), 2974 (m), 2934 (m), 2877 (m), 2238 (w), 2126 (w), 1637(m), 1612 (s), 1586 (m), 1513 (s), 1456 (s), 1420 (s), 1372 (s), 1345 (s), 1301 (s), 1246 (s), 1173 (s), 1093 (s), 1028 (s), 954 (s), 913 (s), 820 (s), 734 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.31 (d, $J = 8.6\text{ Hz}$, 2 H, Ar- H_2 , H_a), 6.87 (d, $J = 8.6\text{ Hz}$, 2 H, Ar- H_2 , H_b), 5.81 (ddd, $J = 17.2, 10.3, 8.3\text{ Hz}$, 1 H, $\text{C}_9\text{-H}$), 5.13 (d, $J = 17.2\text{ Hz}$, 1 H, $\text{C}_{10}\text{-H}_2$, H_c), 5.08 (dd, $J = 7.1, 1.3\text{ Hz}$, 1 H, $\text{C}_3\text{-H}$), 5.02 (d, $J = 10.3\text{ Hz}$, 1 H, $\text{C}_{10}\text{-H}_2$, H_d), 4.64 (d, $J = 10.8\text{ Hz}$, 1 H, one of CH_2Ar), 4.56 (d, $J = 10.8\text{ Hz}$, 1 H, one of CH_2Ar), 3.80 (s, 3 H, ArOCH_3), 3.18 (dd, $J = 6.6, 5.1\text{ Hz}$, 1 H, $\text{C}_7\text{-H}$), 2.82 (m, 1 H, $\text{C}_6\text{-H}$), 2.57 (m, 1 H, $\text{C}_8\text{-H}$), 2.51 (d, $J = 2.2\text{ Hz}$, 1 H, $\text{C}_1\text{-H}$), 2.47 (d, $J = 7.3\text{ Hz}$, 1 H, C_3OH), 1.23 (d, $J = 7.1\text{ Hz}$, 3 H, C_6CH_3), 1.09 (d, $J = 6.8\text{ Hz}$, 3 H, C_8CH_3); ^{13}C NMR (100 MHz, CDCl_3) δ 159.2 (Ar, C-OCH_3), 141.3 (C_9), 130.7 (Ar), 130.7 (Ar'), 129.5 (Ar, C-H_a), 114.8 (C_{10}), 114.8 (C'_{10}), 113.7 (Ar, C-H_b), 87.6 (C_5), 87.6 (C'_5), 85.3 (C_7), 81.5 (C_3), 81.5 (C'_3), 77.2 (C_4), 74.3 (CH_2Ar), 72.1 (C_2), 55.3 (ArOCH_3), 52.2 (C_1), 41.4 (C_8), 41.4 (C'_8), 29.9 (C_6), 17.6 (C_6CH_3), 17.6 ($\text{C}'_6\text{CH}_3$), 15.7 (C_8CH_3), 15.7 ($\text{C}'_8\text{CH}_3$); high resolution mass spectrum (+ESI) m/z 335.1623 [$(\text{M}+\text{Na})^+$; calcd for $\text{C}_{20}\text{H}_{24}\text{O}_3\text{Na}$: 335.1623].

7-(4'-Methoxy-benzyloxy)-6,8-dimethyl-dec-9-ene-1,4-diyn-3-one

To a solution of 7-(4'-methoxy-benzyloxy)-6,8-dimethyl-dec-9-ene-1,4-diyn-3-ol (182 mg, 0.58 mmol) in dichloromethane (5 mL) stirred at $0\text{ }^{\circ}\text{C}$ for 30 min. was added Dess-Martin periodinane (0.37 g, 0.88 mmol). The reaction mixture was allowed to warm to ambient temperature and stirred for 3 h. The reaction mixture was quenched with a 1:1 solution of saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ and saturated aqueous NaHCO_3 (10 mL). The

layers were separated, and the aqueous phase was extracted with diethyl ether (3×10 mL). The combined organic extracts were washed with H_2O (1×10 mL), and brine (1×10 mL), dried over MgSO_4 , filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 $\rightarrow$ 90:10 $\rightarrow$ 80:20) afforded the bis-ynone (157 mg, 86%) as a clear yellow oil: TLC R_f = 0.63 (50% $\text{Et}_2\text{O}/\text{P.E.}$); $[\alpha]_D^{25}$ -18.2 (c 1.03, CHCl_3); IR (neat) 3254 (m), 2977 (m), 2937 (m), 2876 (m), 2213 (s), 2097 (s), 1630 (s), 1613 (s), 1587 (m), 1513 (s), 1456 (s), 1421 (m), 1397 (m), 1373 (m), 1341 (s), 1302 (s), 1247 (s), 1210 (s), 1173 (s), 1149 (s), 1111 (s), 1065 (s), 1033 (s), 954 (s), 918 (s), 821 (s), 727 (s), 682 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.30 (d, J = 8.5 Hz, 2 H, Ar- H_2 , H_a), 6.88 (d, J = 8.5 Hz, 2 H, Ar- H_2 , H_b), 5.80 (ddd, J = 17.1, 10.2, 8.4 Hz, 1 H, C_9 -H), 5.15 (d, J = 17.1 Hz, 1 H, C_{10} - H_2 , H_c), 5.06 (d, J = 10.2 Hz, 1 H, C_{10} - H_2 , H_d), 4.62 (d, J = 10.7 Hz, 1 H, one of CH_2Ar), 4.57 (d, J = 10.7 Hz, 1 H, one of CH_2Ar), 3.81 (s, 3 H, ArOCH_3), 3.26 (m, 1 H, C_7 -H), 3.24 (s, 1 H, C_1 -H), 2.98 (m, 1 H, C_6 -H), 2.57 (m, 1 H, C_8 -H), 1.29 (d, J = 7.1 Hz, 3 H, C_6CH_3), 1.10 (d, J = 6.7 Hz, 3 H, C_8CH_3); ^{13}C NMR (100 MHz, CDCl_3) δ 160.3 (C_3), 159.3 (Ar, C-OCH_3), 140.7 (C_9), 130.3 (Ar), 129.4 (Ar, C-H_b), 115.4 (C_{10}), 113.8 (Ar, C-H_a), 98.7 (C_5), 84.7 (C_7), 83.3 (C_4), 82.3 (C_2), 78.0 (C_1), 74.4 (CH_2Ar), 55.3 (ArOCH_3), 41.6 (C_8), 30.6 (C_6), 16.7 (C_6CH_3), 15.7 (C_8CH_3); high resolution mass spectrum (+ESI) m/z 333.1467 $[(\text{M}+\text{Na})^+]$; calcd for $\text{C}_{20}\text{H}_{22}\text{O}_3\text{Na}$: 333.1467].

7-Hydroxy-6,8-dimethyl-dec-9-ene-1,4-diyn-3-one (14).

To a solution of 7-(4'-methoxy-benzyloxy)-6,8-dimethyl-dec-9-ene-1,4-diyn-3-one (50 mg, 0.16 mmol) in dichloromethane (10 mL) and pH 7 buffer solution (0.5 mL) was added DDQ (55 mg, 0.24 mmol). The reaction mixture was stirred at ambient temperature for 1 h and 30 min. TLC showed starting material to remain. Additional DDQ (55 mg, 0.24 mmol) was added and the reaction was stirred at ambient temperature for 14 h. The reaction mixture was quenched with saturated aqueous NaHCO_3 (10 mL). The layers were separated, and the aqueous phase was extracted with diethyl ether (3×10 mL). The combined organic extracts were washed with H_2O (1×10 mL), and brine (1×10 mL), dried over MgSO_4 , filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 $\rightarrow$ 90:10 $\rightarrow$ 80:20 $\rightarrow$ 70:30 $\rightarrow$ 60:40) afforded **14** (31 mg, 100%) as a clear pale yellow oil: TLC R_f = 0.32 (50% $\text{Et}_2\text{O}/\text{P.E.}$); $[\alpha]_D^{25}$ (c , CHCl_3); IR (neat) 3450 (br, m), 3252 (br, m), 3080 (w), 2979 (m), 2937 (m), 2215 (s), 2097 (s), 1626 (s), 1454 (m), 1421 (m), 1375 (m), 1344 (m), 1210 (s), 1137 (m), 1058 (m), 1036 (m), 981 (s), 913 (s), 863 (w), 837 (m), 726 (s), 677 (s) cm^{-1} ; ^1H NMR (600 MHz, CDCl_3) δ 5.67 (ddd, J = 17.1, 10.3, 8.6 Hz, 1 H, C_9 -H), 5.17 (d, J = 17.1 Hz, 1 H, C_{10} - H_2 , H_a), 5.08 (dd, J = 10.3, 1.3 Hz, 1 H, C_{10} - H_2 , H_b), 3.29 (m, 1 H, C_7 -H), 2.95 (m, 1 H, C_6 -H), 2.41 (m, 1 H, C_8 -H), 1.66 (s, 1 H, C_1 -H), 1.33 (d, J = 7.1 Hz, 3 H, C_6 - CH_3), 1.13 (d, J = 6.7 Hz, 3 H, C_8 - CH_3); ^{13}C NMR (150 MHz, CDCl_3) δ 160.0 (C_3), 139.9 (C_9), 116.3 (C_{10}), 96.7 (C_2), 84.0 (C_4), 82.2 (C_5), 78.4 (C_1), 77.4 (C_7), 43.3

(C₈), 31.2 (C₆), 17.1 (C₆-CH₃), 16.0 (C₈-CH₃); high resolution mass spectrum (+ESI) *m/z* 213.0891 [(M+Na)⁺; calcd for C₁₂H₁₄O₂Na: 213.0891].

Dithiane (16).

To a solution of 7-hydroxy-6,8-dimethyl-dec-9-ene-1,4-diyne-3-one (**14**) (59 mg, 0.31 mmol) and propane-1,3-dithiol (74 mg, 0.68 mmol) in dichloromethane (2 mL) and methanol (2 mL) stirred at -10 °C for 30 min. was added sodium methoxide (37 mg, 0.68 mmol). The reaction mixture was allowed to warm to ambient temperature over 24 h. The reaction mixture was quenched with saturated aqueous NH₄Cl solution (5 mL) and stirred for 10 min. The layers were separated, and the aqueous phase was extracted with diethyl ether (3 × 10 mL). The combined organic extracts were washed with H₂O (1 × 10 mL), and brine (1 × 10 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. Gradient flash chromatography (Petroleum ether/diethyl ether, 100:0 → 90:10 → 80:20 → 70:30 → 60:40) afforded **16** (82 mg, 65%) as a white foam: TLC R_f = 0.49 (50% Et₂O/P.E.); [α]_D²⁵ +3.8 (*c* 1.00, CHCl₃); IR (neat) 3350 (br, m), 3075 (w), 2900 (m), 1638 (w), 1413 (s), 1382 (m), 1341 (m), 1275 (m), 1247 (m), 1163 (m), 1124 (s), 1073 (m), 1019 (s), 907 (s), 873 (m), 840 (m), 779 (m), 752 (m), 660 (m) cm⁻¹; ¹H NMR (600 MHz, CDCl₃) 6.02 (ddd, *J* = 17.2, 10.4, 7.5 Hz, 1 H, C₂-H), 5.95 (s, 1 H, C₈-OH), 5.04 (d, *J* = 17.2 Hz, 1 H, C₁-H₂, H_a), 4.98 (d, *J* = 10.4 Hz, C₁-H₂, H_b), 4.40 (t, *J* = 6.2 Hz, 1 H, C₁₀-H), 3.77 (dd, *J* = 10.4, 2.1 Hz, 1 H, C₄-H), 3.16 (dt, *J* = 14.7, 2.4 Hz, 1 H, one of C₇-H₂), 3.09 (app d, *J* = 14.6 Hz, 1 H, one of SCH₂CH₂CH₂S), 2.93 (dt, *J* = 11.2, 2.5 Hz, 2 H, two of SCH₂CH₂CH₂S), 2.80 (m, 3 H, three of SCH₂CH₂CH₂S), 2.68 (m, 1 H, one of C₇-H₂), 2.40 (t, *J* = 7.1 Hz, 1 H, C₃-H), 2.14 (m, 1 H, two of SCH₂CH₂CH₂S), 2.08 (m, 2 H, two of SCH₂CH₂CH₂S), 2.03 (app dq, *J* = 14.6, 5.8 Hz, 2 H, C₉-H₂), 1.84 (m, 3 H, C₅-H and two of SCH₂CH₂CH₂S), 1.18 (d, *J* = 6.8 Hz, 3 H, C₅CH₃), 0.99 (d, *J* = 7.0 Hz, 3 H, C₃CH₃); ¹³C NMR (150 MHz, CDCl₃) δ 142.5 (C₂), 113.5 (C₁), 95.9 (C₈), 72.1 (C₄), 53.4 (C₆), 47.9 (C₉), 43.5 (C₇), 42.0 (C₅), 41.4 (C₁₀), 38.6 (C₃), 30.7 (SCH₂CH₂CH₂S), 30.7 (SCH₂CH₂CH₂S), 25.8 (SCH₂CH₂CH₂S), 25.7 (SCH₂CH₂CH₂S), 25.5 (SCH₂CH₂CH₂S), 25.1 (SCH₂CH₂CH₂S), 11.9 (C₃CH₃), 11.8 (C₅CH₃); high resolution mass spectrum (+ESI) *m/z* 429.1026 [(M+Na)⁺; calcd for C₁₈H₃₀O₂S₄Na: 429.1026].