Supplemental Information

Rhodium Catalyzed Synthesis of Eight-Member Rings

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Part A: Experimental procedures and tabulated characterization data for new compounds not reported in the experimental section.

All chemicals used were reagent grade. THF was distilled from sodium benzophenone, and CH_2Cl_2 was distilled from CaH_2 . Reactions were monitored by TLC using polyester silica gel 60 F_{254} plates (0.25 mm). . Flash chromatography was performed using 32-63 D, 60 Å silica gel. ^1H NMR spectra were recorded at 300 MHz spectrometer and are reported in PPM relative to TMS. . Coupling constants (J) are reported in Hertz. . ^{13}C NMR spectra were recorded at 75 MHz and are reported in PPM relative to TMS. All reactions, unless otherwise noted, were carried out under N_2 in oven-dried glassware. All reported yields are isolated.

Representative Procedure for the Preparation of Catalyst

To a vial containing $[\text{Rh}(\text{NBD})\text{Cl}]_2$ (75 mg, 0.16 mmol), 2 mL of THF is added. . After stirring for 15 minutes, this orange solution is quickly transferred via cannulae to a vial containing a solution of (S,S)-Me-DuPHOS (98 mg, 0.32 mmol) in 2 mL of THF. . After stirring for 15 minutes, this red solution is transferred via cannulae to a vial containing a solution of AgSbF_6 (56 mg, 0.16 mmol) in 2 mL of THF. . After 15 minutes, this dark suspension is transferred to a tared vial using a syringe fitted with a filter. . The cherry red filtrate is concentrated *en vacuo* and kept under vacuum (<1 mm Hg) overnight to remove all solvent. . 211 mg of orange/red solid were collected. . This catalyst can be stored under nitrogen at 0° C for short period of time.

General Procedure for the [4+2+2] Dimerization of a Dienyne

To a clean, dry 15-mL Schlenk tube, 30 mg of catalyst was added as a solution in 2 mL of CH₂Cl₂. H₂ was gently bubbled through the orange/red solution for 3 minutes causing it to become dark and cloudy, after which 0.5 mL of EtOAc was added followed by sparging with N₂ for 3 minutes. The diyne (0.38 mmol) was then added along with 1 mL of CH₂Cl₂. The reaction was freeze-pump-thawed three times, back-filled with N₂, and stirred overnight at room temp (60 °C for the tosyl amide dienyne). Flash chromatography with 5% EtOAc in hexanes (10% for the tosyl amides) yields the pure product.

The [4+2+2] dimerization to form 8-[(2*E*,4*E*)-Hexa-2,4-dienyloxy]methyl-6-methyl-1,3,3a,6-tetrahydrocycloocta[*c*]furan 3)

To a clean, dry 15-mL Schlenk tube, 30 mg of catalyst was added as a solution in 2 mL of CH₂Cl₂. H₂ was gently bubbled through the orange/red solution for 3 minutes causing it to become dark and cloudy. 0.5 mL of EtOAc was added, and N₂ was gently bubbled through the solution for 3 more minutes. **1** (52mg, 0.38 mmol) was then added along with 1 mL of CH₂Cl₂. The reaction was freeze-pump-thawed three times, back-filled with N₂, and stirred overnight at room temp (60° C for the tosyl amide dienyne). Flash chromatography with 5% EtOAc in hexanes yielded 40 mg (78%) of **3**. ¹H-NMR (300 MHz, CDCl₃) δ 6.19-5.98 (m, 2H), 5.73-5.51 (m, 4H), 5.40 (d, J = 6.6 Hz, 1H), 5.03 (dd, J = 10.0, 5.9 Hz, 1H), 4.42 (d, J = 13.7 Hz, 1H), 4.30 (d, J = 13.7 Hz, 1H), 4.20-4.07 (m, 2H), 3.90 (d, J = 6.1 Hz, 2H), 3.85-3.73 (m, 3H), 1.07 (d, J = 6.7 Hz, 3H); ¹³C-NMR (75 MHz, CDCl₃) δ 149.1, 136.9, 136.8, 133.3, 130.9, 130.8, 129.9, 126.7, 120.8, 117.1, 76.5, 75.2, 74.0, 70.0, 42.4, 32.4, 20.2, 18.1; IR (thin film) 2852.6, 2868.0, 2914.3, 2929.7, 2959.6, 2998.2, 3015.5, 2338.6, 2361.7, 1362.6, 1374.2, 1435.9, 1457.1, 1652.9, 1662.5, 1669.3, 1675.1, 1684.7, 1690.5, 1695.3, 1700.2, 1717.5, 1733.9, 668.3, 937.3, 990.3,

990.4, 1054.0, 1073.3, 110.9, 1139.9 cm^{-1} ; MS-EI m/z (% relative intensity) 272 (M^+ , 4), 174.1 (30), 159.1 (8), 145.1 (21), 133.1 (29), 105.1 (55), 91.7 (57), 81.1 (100), 65.1 (17), 53.1 (28), MS-HREI Calculated for $\text{C}_{18}\text{H}_{24}\text{O}_2$ (M^+) m/e 272.1776, measured m/e 272.1775.

8-[(2E)-Penta-2,4-dienyloxy]methyl-1,3,3a,6-tetrahydrocycloocta[c]furan (5)

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 6.38-6.21 (m, 2H), 6.09 (s, 1H), 5.92 (s, 1H), 5.82-5.71 (m, 2H), 5.34 (d, $J = 10.4$ Hz, 1H), 5.21 (d, $J = 16.8$ Hz, 1H), 5.10 (d, $J = 10.4$ Hz, 1H), 4.35 (s, 2H), 4.12 (dd, $J = 8.2, 7.2$ Hz, 1H), 3.98 (d, $J = 6.6$ Hz, 2H), 3.93 (s, 2H), 3.79 (dd, $J = 5.2, 8.5$ Hz, 1H), 3.45 (s, br, 1H), 2.84 (d, $J = 7.1$ Hz, 2H); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ 142.4, 139.3, 136.6, 133.4, 129.8, 127.7, 124.2, 118.1, 117.8, 76.3, 73.2, 71.6, 70.2, 43.4, 27.5; IR (thin film) 3015.7, 2937.4, 2852.4, 2249.1, 1817.7, 1640.2, 1604.1, 1435.8, 1357.0, 1301.1, 1259.8, 1104.7, 1064.5, 1005.6, 935.9, 908.4, 857.4, 732.3, 649.4, 542.1 cm^{-1} ; MS-HREI Calcd for $\text{C}_{16}\text{H}_{20}\text{O}_2$ (MH^+) m/e 244.1463, measured m/e 244.1475.

7-Penta-2,4-dienyloxymethyl-1,3,3a,6-tetrahydro-cycloocta[c]furan (6)

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 6.38-6.21 (m, 2H), 6.09 (s, 1H), 5.92 (s, 1H), 5.82-5.71 (m, 2H), 5.34 (d, $J = 10.4$ Hz, 1H), 5.21 (d, $J = 16.8$ Hz, 1H), 5.10 (d, $J = 10.4$ Hz, 1H), 4.35 (s, 2H), 4.12 (dd, $J = 8.2, 7.2$ Hz, 1H), 3.98 (d, $J = 6.6$ Hz, 2H), 3.93 (s, 2H), 3.79 (dd, $J = 5.2, 8.5$ Hz, 1H), 3.45 (s, br, 1H), 2.84 (d, $J = 7.1$ Hz, 2H); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ 142.4, 139.3, 136.6, 133.4, 130.4, 129.8, 127.7, 124.2, 118.1, 117.8, 76.3, 73.2, 71.6, 70.2, 43.4, 27.5; IR (thin film) 3015.7, 2937.4, 2852.4, 2249.1, 1817.7, 1640.2, 1604.1, 1435.8, 1357.0, 1301.1, 1259.8, 1104.7, 1064.5, 1005.6, 935.9, 908.4, 857.4, 732.3, 649.4, 542.1 cm^{-1} ; MS-HREI Calculated for $\text{C}_{16}\text{H}_{20}\text{O}_2$ (MH^+) m/e 244.1463, measured m/e 244.1475.

***N*-[(2-Toluenesulfonyl-7-methyl-2,3,7,9a-tetrahydro-1*H*-cycloocta[c]pyrrol-5-yl)methyl]-*N*-toluenesulfonyl-hexa-2,4-dien-1-amide (8)**

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 7.70 (d, $J = 8.2$ Hz, 2H), 7.62 (d, $J = 8.2$ Hz, 2H), 7.36 (d, $J = 8.5$ Hz, 2H), 7.26 (d, $J = 8.5$ Hz, 2H), 5.86 (dt, $J = 10.2, 24.7$ Hz, 2H), 5.63-5.54 (m, 2H), 5.47 (ddd, $J = 9.9, 9.9, 2.2$ Hz, 1H), 5.22 (d, $J = 6.9$ Hz, 1H), 5.08 (dt, $J = 14.1, 7.1$ Hz, 1H), 4.93 (dd, $J = 10.2, 6.0$ Hz, 1H), 4.00 (s, br, 1H), 3.89 (d, $J = 14.4$ Hz, 1H), 3.71-3.57 (m, 5H), 3.47 (d, $J = 13.8$ Hz, 1H), 2.91 (t, $J = 8.7$ Hz, 1H), 2.44 (s, 3H), 2.42 (s, 3H), 1.70 (d, $J = 6.9$ Hz, 3H), 0.99 (d, $J = 6.9$ Hz, 3H); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ 145.1, 143.8, 143.2, 138.3, 137.2, 134.6, 132.1, 130.3, 130.2, 129.8, 129.6, 128.5, 127.9, 127.1, 123.8, 121.4, 120.4, 120.0, 54.7, 54.6, 48.1, 41.2, 32.7, 21.5, 21.4, 19.9, 18.0; IR (neat) 3402.1, 2924.2, 2869.7, 2584.7, 2254.5, 1920.8, 1694.0, 1596.8, 1493.8, 1450.9, 1340.1, 1160.0, 1092.1, 1042.3, 1016.9, 990.3, 912.0, 814.9, 732.0, 707.8, 664.3, 580.4, 549.0 cm^{-1} ; MS-HREI Calcd for $\text{C}_{32}\text{H}_{38}\text{N}_2\text{O}_4\text{S}_2\text{Li}$ (M^+) m/e 585.2433, measured m/e 585.2425.

7-[(3E)-Hexa-3,5-dienyloxy]methyl-1,3,4,5,9,11a-hexahydrocycloocta[c]oxepine (10)

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 6.30 (dt, $J = 16.8, 10.4$ Hz, 1H), 6.09 (d, $J = 10.4$ Hz, 1H), 5.95 (s, 1H), 5.76-5.60 (m, 2H), 5.48 (s, 1H), 5.32 (t, $J = 6.9$ Hz, 1H), 5.10 (d, $J = 17.0$ Hz, 1H), 4.98 (d, $J = 9.89$ Hz, 1H), 4.10 (d, $J = 4.9$ Hz, 1H), 3.97 (d, $J = 7.4$ Hz, 2H), 3.90 (d, $J = 6.0$ Hz, 1H), 3.56 (t, $J = 11.3$ Hz, 1H), 3.44 (td, $J = 6.9, 6.9$ Hz, 2H), 3.36 (s, br, 1H), 2.83-2.66 (m, 1H), 2.66-2.54 (m, 1H), 2.36 (ddd, $J = 6.9, 6.9, 6.9$ Hz, 1H), 2.07-1.95 (m, 1H), 1.63 (d, $J = 13.7$ Hz, 1H); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): δ 138.4, 137.3, 132.9, 131.5, 131.2, 125.1, 121.5, 120.2, 115.7, 70.0, 69.9, 69.7, 64.6, 33.3, 28.4; IR (thin film) 3299.8, 3087.2, 3012.0, 2923.2, 2851.9, 2245.4, 1690.9, 1652.1, 1631.1, 1603.1, 1438.4, 1355.9, 1305.5, 1265.8, 1222.9, 1210.1, 1094.5, 1059.2, 1005.6, 951.2, 909.1, 862.9, 842.7, 734.6, 668.2, 629.5, 595.0 cm^{-1} ; MS-HREI Calcd for $\text{C}_{18}\text{H}_{24}\text{O}_2$ (M^+) m/e 272.1776, measured m/e 272.1776.

8{[(2E, 4E)-3-Methyl-hexa-2, 4-dienyloxy]methyl} 4, 6-dimethyl-1, 3, 3a, 6-tetrahydrocycloocta[c]furan (14)

^1H NMR (300 MHz, CDCl_3) δ 6.07 (d, J = 15.1 Hz, 1H), 5.71-5.64 (m, 2H), 5.46 (t, J = 6.4 Hz, 1H), 5.40 (d, J = 5.2 Hz, 1H), 5.22 (d, J = 9.3 Hz, 1H), 4.38 (d, J = 12.6 Hz, 1H), 4.25 (d, J = 12.6 Hz, 1H), 4.05-3.93 (m, 5H), 3.90-3.82 (m, 1H), 3.78 (s, 2H), 1.77 (d, J = 6.6 Hz, 3H), 1.74 (s, 3H), 1.72 (s, 3H), 1.06 (d, J = 6.0 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 149.6, 139.2, 137.2, 135.4, 131.5, 130.2, 125.4, 124.7, 123.8, 117.1, 77.4, 74.2, 71.8, 65.9, 45.0, 31.6, 21.2, 20.1, 18.6, 13.0; MS-HRES Calculated for $\text{C}_{20}\text{H}_{28}\text{O}_2$ (M^+Na) m/e 323.1987, measured m/e 323.1990. This sample contained approximately 15% of the other diastereomer of this structure.

8{[(2E, 4E)-4-Methyl-hexa-2, 4-dienyloxy]methyl} 5, 6-dimethyl-1, 3, 3a, 6-tetrahydrocycloocta[c]furan (16)

^1H NMR (300 MHz, CDCl_3) δ 6.22 (d, J = 15.6 Hz, 1H), 6.19 (d, J = 15.4 Hz, 1H), 5.79 (broad s, 1H), 5.69 (broad s, 1H), 5.63-5.50 (m, 4H), 5.48-5.39 (m, 2H), 4.80 (broad s, 2H), 4.54 (d, J = 14.1 Hz, 1H), 4.48 (d, J = 13.7 Hz, 1H), 4.37 (d, J = 14.5 Hz, 1H), 4.28 (d, J = 13.4 Hz, 1H), 4.20-4.08 (m, 6H), 3.99 (d, J = 5.77 Hz, 2H), 3.94 (d, J = 6.3 Hz, 2H), 3.78 (s, 4H), 3.56 (dd, J = 7.4, 8.8 Hz, 1H), 3.36 (dd, J = 8.5, 9.3 Hz, 1H), 1.73 (s, 12H), 1.72 (d, J = 6.3 Hz, 6H), 1.12 (d, J = 6.8 Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 150.0, 144.1, 137.8, 137.8, 130.7, 127.2, 126.4, 122.1, 120.1, 116.9, 116.3, 113.4, 111.9, 76.1, 75.4, 74.3, 74.2, 71.8, 70.9, 70.4, 69.6, 49.4, 43.2, 42.7, 35.1, 31.6, 22.7, 18.4, 17.5, 13.9, 12.1.; MS-HRES Calculated for $\text{C}_{20}\text{H}_{28}\text{O}_2$ (M^+Na) m/e 323.1987, measured m/e 323.1985.

General Procedure for the [4+2+2] Co-cyclization of a Dienyne and Terminal Alkyne

To a clean, dry 15-mL Schlenk tube, 30 mg of catalyst was added as a solution in 2 mL of CH_2Cl_2 . H_2 was gently bubbled through the orange/red solution for 3 minutes causing it to become dark and cloudy. 0.5 mL of EtOAc was added, followed by sparging with N_2 for 3 minutes. The terminal alkyne (1.9 mmol) was added along with 0.5 mL of CH_2Cl_2 , and the reaction was stirred to ensure homogeneity. Finally, the dienyne (0.38 mmol) was added along

with 0.5 mL of CH₂Cl₂. The reaction was freeze-pump-thawed three times, back-filled with N₂, and stirred overnight in a 60 °C oil bath. . Flash chromatography with 5% or 10% EtOAc in hexanes provided the pure product.

8-[(Benzyloxy)methyl]-6-methyl-1,3,3a,6-tetrahydrocycloocta[c]furan (20)

To a clean, dry 15-mL Schlenk tube, 30 mg of catalyst was added as a solution in 1 mL of CH₂Cl₂. H₂ was gently bubbled through the orange/red solution for 3 minutes causing it to become dark and cloudy. . 0.5 mL of EtOAc was added, and N₂ was gently bubbled through the solution for 3 more minutes. Benzyl propargyl ether (278mg, 1.9 mmol) was added with 1 mL of CH₂Cl₂. **1** (47 mg, 0.38 mmol) was then added along with 1 mL of CH₂Cl₂. The reaction was freeze-pump-thawed three times, back-filled with N₂, and stirred overnight 60 °C. Flash chromatography with 5% EtOAc in hexanes yielded 76.3 mg (73%) of **20**. ¹H-NMR (300 MHz, CDCl₃) δ 7.38-7.26 (m, 5H), 5.79 (dd, J = 2.5 Hz, 1H), 5.60 (ddd, J = 9.5, 9.5, 2.2, 1H), 5.44 (d, J = 6.6 Hz, 1H), 5.07 (ddd, J = 9.9, 5.5, 1.1 Hz, 1H), 4.47 (m, 3H), 4.31 (d, J = 13.5 Hz, 1H), 4.21 (t, J = 7.7 Hz, 1H), 4.17-4.11 (m, 1H), 3.86 (s, 2H), 3.82-3.80 (m, 1H), 3.66 (t, J = 7.7 Hz, 1H), 1.11 (d, J = 6.9 Hz, 3H); ¹³C-NMR (75 MHz, CDCl₃) δ 149.2, 138.2, 137.1, 136.9, 130.7, 128.3, 127.8, 127.5, 120.7, 117.1, 76.6, 75.2, 74.0, 71.4, 42.4, 32.4, 20.2; IR (thin film) 3305.8, 3065.7, 3030.7, 2939.6, 2856.1, 2247.2, 1952.3, 1731.7, 1640.1, 1496.3, 1454.0, 1357.7, 1357.7, 1311.7, 1249.4, 1206.2, 1161.2, 1069.0, 1028.0, 924.6, 909.1, 845.7, 733.1, 698.2, 605.6, 542.2, 464.2 cm⁻¹; MS-HREI Calcd for C₁₈H₂₀O₂Li (MLi⁺) m/e 275.1623, measured m/e 275.1620.

8-[(Allyloxy)methyl]-6-methyl-1,3,3a,6-tetrahydrocycloocta[c]furan (22)

¹H-NMR (500 MHz, CDCl₃) δ 5.90 (m, 1H), 5.76 (d, J = 2.0 Hz, 1H), 5.58 (ddd, J = 9.6, 9.6, 1.9 Hz, 1H), 5.43 (d, J = 6.5 Hz, 1H), 5.26 (dd, J = 17.5, 2.0 Hz, 1H), 5.18 (dd, J = 10.5, 1.5 Hz, 1H), 5.07 (dd, J = 10.0, 6.0 Hz, 1H), 4.46 (d, J = 14.0 Hz, 1H), 4.32 (d, J = 14.0 Hz, 1H), 4.20 (t, J = 7.5 Hz, 1H), 4.14-4.12 (s, br, 1H), 3.92 (d, J = 6.0 Hz, 2H), 3.85-3.77 (m, 3H), 3.66 (dd = 7.7 Hz, 1H), 1.09 (d, J = 6.7 Hz, 3H); ¹³C-NMR (125 MHz, CDCl₃) δ 149.1, 136.9, 136.8, 134.8, 130.8,

120.7, 117.1, 117.1, 76.5, 75.1, 74.0, 70.5, 47.3, 32.3, 20.1; IR (thin film) 2928.6, 2855.9, 2250.6, 1726.9, 1452.7, 1351.3, 1261.8, 1069.8, 991.1, 909.4, 732.1, 648.6 cm^{-1} ; UV-Vis (MeOH) $\lambda_{\text{max}} = 274 \text{ nm}$, $\epsilon = 1.1960 \times 10^4$, $1.629 \times 10^{-5} \text{ M}$; MS-HREI Calcd for $\text{C}_{15}\text{H}_{20}\text{O}_2$ (MH^+) m/e 232.1463, measured m/e 232.1474.

8-[(Trimethylsiloxy)methyl]-6-methyl-1,3,3a,6-tetrahydrocycloocta[c]furan (24)

^1H -NMR (300 MHz, CDCl_3) δ 5.77 (d, $J = 2.4 \text{ Hz}$, 1H), 5.59 (ddd, $J = 9.8, 9.3, 2.2 \text{ Hz}$, 1H), 5.46 (d, $J = 6.6 \text{ Hz}$, 1H), 5.08 (ddd, $J = 10.0, 5.5, 1.1 \text{ Hz}$, 1H), 4.47 (d, $J = 13.7$, 1H), 4.32 (d, $J = 13.7$, 1H), 4.21 (t, $J = 7.7 \text{ Hz}$, 1H), 4.15–4.05 (s, br, 1H), 3.98 (s, 2H), 3.66 (t, $J = 7.8$, 1H), 3.48 (q, $J = 7.1 \text{ Hz}$, 1H), 1.12 (d, $J = 6.6 \text{ Hz}$, 3H); ^{13}C -NMR (75 MHz, CDCl_3) δ 148.8, 137.0, 134.4, 132.7, 120.5, 116.7, 75.2, 74.0, 68.9, 42.3, 32.2, 20.2, 15.2, -0.3; IR (thin film) 3309.7, 3015.9, 2958.4, 2902.7, 2853.1, 1740.4, 1651.9, 1456.7, 1374.0, 1320.2, 1251.2, 1140.6, 1094.7, 1073.1, 959.5, 939.5, 870.8, 842.8, 739.3, 706.3, 666.7, 635.3, 537.4 cm^{-1} ; MS-HREI Calcd for $\text{C}_{15}\text{H}_{24}\text{O}_2\text{Si}$ (M^+) m/e 264.1546, measured m/e 264.1498. Sample was labile and so the TMS group was removed and the MS-HREI was run on the free alcohol, Calcd for $\text{C}_{15}\text{H}_{16}\text{O}_2$ (M^+) m/e 192.1150, measured m/e 192.1150.

6-Methyl-8-propyl-1,3,3a,6-tetrahydrocycloocta[c]furan (26)

^1H -NMR (300 MHz, CDCl_3) δ 5.67 (s, 1H), 5.62 (ddd, $J = 9.5, 9.5, 2.4 \text{ Hz}$, 1H), 5.21 (d, $J = 6.9 \text{ Hz}$, 1H), 5.05 (ddd, $J = 10.2, 5.1, 0.9 \text{ Hz}$, 1H), 4.45 (d, $J = 13.2 \text{ Hz}$, 1H), 4.33 (dt, $J = 13.2, 2.4 \text{ Hz}$, 1H), 4.20 (t, $J = 7.8 \text{ Hz}$, 1H), 4.05–4.02 (s, br, 1H), 3.68 (t, $J = 7.8 \text{ Hz}$, 1H), 1.94 (t, $J = 7.7 \text{ Hz}$, 2H), 1.31–1.29 (m, 2H), 1.06 (d, $J = 6.9 \text{ Hz}$, 1H), ^{13}C -NMR (75 MHz, CDCl_3) δ 133.3, 130.8, 130.1, 126.5, 118.6, 117.5, 79.7, 79.0, 74.3, 70.5, 36.0, 35.3, 23.7, 18.1; IR (thin film) 3133.7, 2960.6, 2929.9, 2857.2, 2253.2, 1794.3, 1648.5, 1457.7, 1378.4, 1261.5, 1080.8, 908.6, 734.5, 650.7 cm^{-1} ; MS-HREI Calcd for $\text{C}_{14}\text{H}_{20}\text{O}$ (MH^+) m/e 204.1514, measured m/e 204.1512.

6-[(Benzyloxy)methyl]-3,4,8,10a-tetrahydro-1H-cycloocta[c]pyran (27)

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 7.36-7.25 (m, 5H), 5.98 (s, 1H), 5.70-5.63 (m, 1H), 5.49 (m, 1H), 5.39 (t, $J = 7.3$ Hz, 1H), 4.51 (d, $J = 2.7$ Hz, 2H), 4.12 (d, $J = 5.8$ Hz, 1H), 4.05 (d, $J = 5.5$ Hz, 2H), 3.99 (s, br, 1H), 3.57 (t, $J = 12.1$ Hz, 1H), 3.41 (s, br, 1H), 2.84-2.58 (m, 2H), 2.11-2.18 (m, 1H), 1.65 (d, $J = 13.7$ Hz, 1H); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ 138.3, 136.8, 131.3, 128.6, 128.0, 127.9, 127.8, 127.5, 126.9, 125.5, 121.5, 120.6, 74.1, 72.4, 69.7, 64.6, 33.5, 32.9, 28.5; IR (thin film) 3300.9, 3011.0, 2922.1, 2849.9, 2744.4, 2245.7, 1951.5, 1873.0, 1809.2, 1732.7, 1630.7, 1469.3, 1453.9, 1438.3, 1356.4, 1305.3, 1265.2, 1222.2, 1095.2, 1059.3, 1028.3, 1005.6, 949.6, 863.3, 843.8, 789.0, 728.7, 698.1, 628.9, 595.1 cm^{-1} ; MS-HREI Calcd for $\text{C}_{18}\text{H}_{24}\text{O}_2$ (M^+) m/e 272.1776, measured m/e 272.1776.

8-[(Benzyloxy)methyl]-6-methyl-2-tolunesulfonyl-2,3,3a,6-tetrahydro-1H-cycloocta[c]pyrrole (29)

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 7.71 (d, $J = 8.2$ Hz, 2H), 7.34 (d, $J = 8.2$ Hz, 2H), 7.32-7.25 (m, 5H), 5.75 (d, $J = 2.2$ Hz, 1H), 5.55 (ddd, $J = 10.2, 9.1, 2.2$ Hz, 1H), 5.44 (d, $J = 6.9$ Hz, 1H), 4.97 (ddd, $J = 10.2, 5.5, 1.0$ Hz, 1H), 4.4 (s, 2H), 4.14-4.02 (m, 2H), 4.00 (d, $J = 14.4$ Hz, 1H), 3.79 (s, 2H), 3.71 (d, $J = 14.4$ Hz, 1H), 3.62 (dd, $J = 16.6, 7.7$ Hz, 1H), 2.95 (dd, $J = 8.6, 8.6$ Hz, 1H), 1.06 (d, $J = 6.9$ Hz, 1H); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ 144.9, 144.1, 138.4, 137.9, 137.5, 132.2, 131.5, 130.0, 128.6, 128.2, 128.1, 127.9, 121.7, 120.6, 76.3, 71.7, 55.0, 54.6, 41.4, 33.1, 21.8, 20.2; IR (thin film) 3278.2, 3062.2, 3027.4, 2957.5, 2925.5, 2855.1, 2735.6, 2584.6, 2502.4, 2414.1, 2253.6, 1950.9, 1921.4, 1873.5, 1810.6, 1716.4, 1651.7, 1597.5, 1494.5, 1472.7, 1454.5, 1397.7, 1337.8, 1290.1, 1152.6, 1098.0, 911.2, 815.9 cm^{-1} ; MS-HRFAB Calcd for $\text{C}_{26}\text{H}_{29}\text{NO}_3\text{S}$ ($\text{M}+\text{Li}^+$) m/e 442.2050, measured m/e 442.2040.

N-[(2-Tolunesulfonyl-7-methyl-2,3,7,9a-tetrahydro-1H-cycloocta[c]pyrrol-5-yl)methyl]-N-tolunesulfonamide (31)

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 7.76-7.62 (m, 4H), 7.36-7.24 (m, 4H), 5.49 (d, $J = 2.5$ Hz, 1H), 5.41 (ddd, $J = 10.2, 9.0, 2.4$ Hz, 1H), 5.27 (d, 7.5 Hz, 1H), 4.88 (ddd, $J = 10.2, 5.1, 0.9$ Hz, 1H), 4.73 (t, $J = 6.2$ Hz, 1H), 3.87-3.77 (m, 2H), 3.58 (d, $J = 16.5$ Hz, 1H), 3.48 (dd, $J = 17.4$ Hz, 7.5 Hz, 2H), 3.35 (d, $J = 6.3$ Hz, 2H), 2.89 (dd, $J = , 9.1, 9.1$ Hz, 1H), 2.43 (s, 3H), 2.40 (s, 3H), 0.94 (d, $J = 6.9$ Hz, 3H); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ 145.3, 144.0, 143.5, 137.2, 137.1, 136.9, 131.8, 129.8, 129.6, 127.9, 127.4, 127.3, 121.8, 119.8, 54.6, 54.1, 51.3, 41.0, 32.8, 21.5, 19.7; IR (neat) 3284.0, 2924.8, 2870.4, 2586.5, 2345.4, 2249.8, 1923.5, 1923.5, 1734.1, 1654.3, 1597.1, 1542.4, 1493.7, 1449.7, 1332.8, 1332.8, 1115.2, 1092.4, 1044.8, 815.0, 707.4, 664.0, 582.6, 549.5, 414.1 cm^{-1} ; MS-HREI Calcd for $\text{C}_{20}\text{H}_{26}\text{NO}_3\text{S}$ (MH^+) m/e 360.1633, measured m/e 360.1640.

6-[(Benzyloxy)methyl]-2-toluenesulfonyl-1,2,3,4,8,10a-hexahydrocycloocta[c]pyridine (33)

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 7.66 (d, $J = 8.2$ Hz, 2H), 7.38-7.26 (m, 7H), 6.06 (s, 1H), 5.59-5.50 (m, 1H), 5.37 (t, $J = 6.9$, 1H), 5.27-5.20 (m, 1H), 4.49 (s, 2H), 4.11 (dd, $J = 9.6, 13.2$ Hz, 1H), 3.99 (s, 2H), 3.69 (d, $J = 11.5$ Hz, 1H), 3.33 (s, br, 1H), 2.96 (d, $J = 13.5$ Hz, 1H), 2.81-2.65 (m, 1H), 2.60-2.46 (m, 2H), 2.41 (s, 3H), 2.00-1.89 (m, 1H), 1.71 (d, $J = 13.7$ Hz, 1H); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ 143.8, 138.5, 138.4, 133.5, 133.3, 130.4, 130.2, 129.9, 128.6, 128.1, 128.0, 127.9, 127.8, 127.7, 125.5, 124.2, 120.7, 49.4, 33.3, 31.0, 28.3, 21.8; IR (thin film) 3405.3, 3307.8, 3154.9, 3013.0, 2926.6, 2856.0, 2736.1, 2254.2, 1919.0, 1797.0, 1729.4, 1630.3, 1598.2, 1495.1, 1454.5, 1442.0, 1348.5, 1332.0, 1237.0, 1208.1, 1165.0, 1092.4, 1044.0, 969.8, 942.3, 908.1, 846.6, 815.0, 732.5, 698.9, 661.7, 649.1, 550.0 cm^{-1} ; MS-HRFAB Calcd for $\text{C}_{26}\text{H}_{29}\text{NO}_3\text{SLi}$ ($\text{M}+\text{Li}^+$) m/e 442.2050, measured m/e 442.2040.

10-(Benzyloxymethyl)-8-methyl-5,5a,8,12-tetrahydrocycloocta[b]naphthalene (36)

This reaction is performed with 58 mg (0.28 mmol) of dienyne, and is purified by flash chromatography (CH₂Cl₂/Et₂O/hexanes: 1/1/80). . All other aspects of the general procedure were followed: ¹H-NMR (300 MHz, CDCl₃) δ 7.55 – 7.26 (m, 9H), 5.59 (s, br, 1H), 5.59-5.50 (m, 1H), 5.35 (t, J = 6.7, 1H), 5.27-5.20 (m, 1H), 4.44 (s, 2H), 4.32 (s, 2H), 4.10-3.93 (m, 3H), 3.50-3.28 (m, br, 4H); ¹³C-NMR (75 MHz, CDCl₃) δ 137.2, 136.7, 137.5, 132.2, 131.7, 130.3, 129.6, 128.7, 128.4, 128.2, 127.8, 127.5, 126.9, 125.5, 121.5, 120.6, 76.5, 75.1, 33.3, 31.0, 28.3, 21.8; IR (thin film) 3292.2, 3064.2, 2856.3, 2116.27, 1954.4, 1880.0, 1812.3, 1725.0, 1495.9, 1454.2, 1354.9, 1263.6, 1075.0, 911.4, 737.9, 698.0 cm⁻¹; MS-HREI Calcd for C₂₄H₂₄O m/e 328.1827, observed m/e 328.1824.

8{[benzyloxy]methyl} 4, 6-dimethyl-1, 3, 3a, 6-tetrahydrocycloocta[c]furan (39)

¹H NMR (300 MHz, CDCl₃) δ 7.34-7.24 (m, 5H), δ 5.69 (d, J = 2.2 Hz, 1H), δ 5.41 (d, J = 4.9 Hz, 1H), δ 5.23 (d, J = 8.8 Hz, 1H), δ 4.59-4.23 (m, 3H), δ 4.38 (d, J = 12.6 Hz, 1H), δ 4.25 (d, J = 13.7 Hz, 1H), δ 4.00 (dd, J = 7.1 Hz, 3.5 Hz, 2H), δ 3.99-3.82 (m, 3H), δ 1.73 (s, 3H), δ 1.07 (d, J = 6.6 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 149.7, 139.3, 131.5, 130.0, 128.5, 128.1, 127.9, 127.7, 117.0, 77.5, 74.2, 71.8, 71.6, 45.0, 31.6, 21.2, 20.1; MS-HREI Calculated for C₂₀H₂₄O₂ (M+NA) m/e 319.1674, measured m/e 319.1675

8{[benzyloxy]methyl} 5,6-dimethyl-1, 3, 3a, 6-tetrahydrocycloocta[c]furan (40)

¹H NMR (300 MHz, CDCl₃) δ 7.41-7.25 (m, 10H), δ 5.81 (broad s, 1H), δ 5.71 (broad s, 1H), δ 5.45 (d, J = 7.4 Hz, 1H), δ 5.40 (broad s, 1H), δ 5.28 (q, J = 6.6 Hz, 1H), δ 4.81 (d, J = 4.95 Hz, 1H), δ 4.66-4.42 (m, 6H), δ 4.38 (d, J = 14.8 Hz, 1H), δ 4.27 (d, J = 13.7 Hz, 1H), δ 4.20-4.04

(m, 4H), δ 3.99 (d, J = 7.1 Hz, 1H), δ 3.96 (d, J = 6.8 Hz, 1H), δ 3.82 (s, 4H), δ 3.55, (t, J = 7.4 Hz, 1H). δ 3.36 (t, J = 8.2 Hz, 1H), δ 1.71 (s, 3H), δ 1.63 (s, 3H), δ 1.58 (d, J = 6.6 Hz, 3H), δ 1.12 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 151.8, 145.7, 139.6, 138.4, 133.1, 132.2, 129.8, 129.4, 129.3, 129.0, 128.6, 128.1, 127.8, 118.5, 117.9, 117.3, 116.6, 114.9, 113.7, 76.6, 75.7, 74.6, 73.5, 73.4, 72.9, 72.3, 71.6, 71.2, 69.9, 51.0, 49.7, 44.8, 44.3, 43.0, 36.8, 35.5, 20.0, 19.1, 18.8, 17.8. MS-HRES Calculated for $\text{C}_{20}\text{H}_{24}\text{O}_2$ (M^+Na) m/e 319.1674, measured m/e 319.1676. Two diastereomers of the product are present.

General Procedure for the [4+2+2] Co-cyclization of a Dienyne and Acetylene

To a clean, dry 15 mL Schlenk tube equipped with a stir bar $\text{Rh}/\text{DuPHOS}/\text{SbF}_6$ (30 mgs) was added as a solution in CH_2Cl_2 (2 mL). The solution was stirred at room temperature while ethyl acetate ($\frac{1}{2}$ mL) was added via syringe. The diyne (0.38 mmol) was added as a solution in CH_2Cl_2 (1 mL) and the tube was sealed. The tube was then put through a freeze-pump-thaw cycle three times and placed in an ice bath. Acetylene was then bubbled through the solution for 5 minutes and the tube was once again sealed and stirred overnight in a 60°C oil bath. The reaction mixture was then concentrated and flash chromatography (10% ethyl acetate in hexanes) afforded the pure product.

6-Methyl-1,3,3a,6-tetrahydrocycloocta[c]furan (43)

^1H NMR (300 MHz, CDCl_3) δ 5.67 (dd, J = 7.7, 2.2 Hz, 1H), δ 5.50 (d, J = 13.4 Hz, 1H), δ 5.47 (d, J = 10.1 Hz, 1H), δ 5.32 (dd, J = 11.8 Hz, 5.7 Hz, 1H), δ 5.05 (dd, J = 9.9, 6.3 Hz, 1H), δ 4.39 (d, J = 13.4 Hz, 1H), δ 4.26 (d, J = 14.0 Hz, 1H), δ 4.23-4.16 (m, 2H), δ 3.83-3.76 (m, 1H), δ 3.69-3.61 (m, 1H), δ 1.10 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 149.5, 139.1, 135.3, 122.4, 120.7, 115.5, 75.2, 73.8, 41.9, 32.3, 20.4. MS-HRES Calculated for $\text{C}_{11}\text{H}_{14}\text{O}$ (M^+Na) m/e 185.0942, measured m/e 185.0945.

4,6-Dimethyl-1,3,3a,6-tetrahydro-cycloocta[c]furan (44)

^1H NMR (300 MHz, CDCl_3) δ 5.59 (d, J = 7.7 Hz, 1H), δ 5.46 (dd, J = 14.3, 7.7 Hz, 1H), δ 5.34 (dd, J = 11.8, 4.6 Hz, 1H), δ 5.14 (d, J = 8.8 Hz, 1H), δ 4.39 (broad s, 1H), δ 4.31 (d, J = 13.7 Hz,

1H), δ 4.23 (d, J = 13.7 Hz, 1H), δ 4.07 (dd, J = 9.0, 5.5 Hz, 1H), δ 3.97 (dd, J = 9.0, 7.4 Hz, 1H), δ 3.79 (broad s, 1H), δ 1.76 (s, 3H), δ 1.07 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 149.7, 140.5, 129.4, 128.3, 122.3, 115.1, 73.3, 71.3, 44.1, 31.3, 21.2, 19.3. . MS-HRES Calculated for $\text{C}_{12}\text{H}_{16}\text{O}$ (M^+Na) m/e 199.1099, measured m/e 199.1097.

5-6-Dimethyl-1,3,3a,6-tetrahydro-cycloocta[*c*]furan (45)

^1H NMR (300 MHz, CDCl_3) δ 5.99-5.94 (m, 1H), δ 6.73 (dd, J = 4.9, 2.4 Hz, 1H), δ 5.63 (dd, J = 7.4, 1.9 Hz, 1H), δ 5.48-5.26 (m, 4H), δ 4.80 (d, J = 4.1 Hz, 1H), δ 4.54 (d, J = 14.5 Hz, 1H), δ 4.44 (d, J = 13.7, 1H), δ 4.36 (d, J = 14.9 Hz, 1H), δ 4.26 (d, J = 6.8 Hz, 1H), δ 4.23-4.07 (m, 5H), δ 3.56 (t, J = 7.1 Hz, 1H), δ 3.37 (t, J = 8.5 Hz, 1H), δ 2.94-2.80 (m, 2H), δ 1.72 (s, 3H), δ 1.63 (s, 3H), δ 1.59 (d, J = 6.6 Hz, 3H), δ 1.13 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 150.8, 149.5, 142.8, 140.0, 129.0, 125.1, 122.5, 120.0, 116.2, 115.5, 112.7, 112.6, 75.4, 74.3, 74.1, 69.6, 49.2, 42.7, 42.2, 35.1, 18.1, 17.4, 14.0, 13.4. . MS-HRES Calculated for $\text{C}_{12}\text{H}_{16}\text{O}$ (M^+Na) m/e 199.1099, measured m/e 199.1098.

Determination of stereochemistry

The determination of which diastereomer we obtained was accomplished by assignment of the ^1H spectra and then examination of the appropriate NOE data. As can be seen in the figures below H_a and H_d are in decidedly different orientations in the two diastereomers.

Observed diastereomer has H_a and H_d near each other. Distance between protons 2.07 Å

Diastereomer not observed has H_a and H_d are on opposite sides of the ring

8-[(Allyloxy)methyl]-6-methyl-1,3,3a,6-tetrahydrocycloocta[*c*]furan

^1H -NMR (500 MHz, CDCl_3) δ 5.90 (m, 1H), 5.76 (d, $J = 2.0$ Hz, 1H), 5.58 (ddd, $J = 9.6, 9.6, 1.9$ Hz, 1H), 5.43 (d, $J = 6.5$ Hz, 1H), 5.26 (dd, $J = 17.5, 2.0$ Hz, 1H), 5.18 (dd, $J = 10.5, 1.5$ Hz, 1H), 5.07 (dd, $J = 10.0, 6.0$ Hz, 1H), 4.46 (d, $J = 14.0$ Hz, 1H), 4.32 (d, $J = 14.0$ Hz, 1H), 4.20 (t, $J = 7.5$ Hz, 1H), 4.14-4.12 (s, br, 1H), 3.92 (d, $J = 6.0$ Hz, 2H), 3.85-3.77 (m, 3H), 3.66 (dd, $J = 7.7$ Hz, 1H), 1.09 (d, $J = 6.7$ Hz, 3H); ^{13}C -NMR (125 MHz, CDCl_3) δ 149.1, 136.9, 136.8, 134.8, 130.8, 120.7, 117.1, 117.1, 76.5, 75.1, 74.0, 70.5, 47.3, 32.3, 20.1; IR (thin film) 2928.6, 2855.9, 2250.6, 1726.9, 1452.7, 1351.3, 1261.8, 1069.8, 991.1, 909.4, 732.1, 648.6 cm^{-1} ; UV-Vis (MeOH) $\lambda_{\text{max}} = 274$ nm, $\epsilon = 1.1960 \times 10^4$, 1.629×10^{-5} M; MS-HREI Calcd for $\text{C}_{15}\text{H}_{20}\text{O}_2$ (MH^+) m/e 232.1463, measured m/e 232.1474.

The complete assignment of the ^1H and ^{13}C spectra was performed. The diastereomer shown was assigned by observation of the nuclear Overhauser effect between the hydrogens on carbons **a** and **d**. Molecular modeling indicates that these two protons are in close proximity to each other in the diastereomer shown.

Carbon #	^1H -Shift	^{13}C -Shift	Type	Selected NOE correlations
k	1.11	20.1	CH_3	5.44
j	3.67	75.1	CH_2	
d	3.82	32.3	CH	4.13
l	3.82	76.5	CH_2	5.76
m	3.93	70.5	CH_2	
a	4.13	42.3	CH	3.82, 5.07
j'	4.20	75.1	CH_2	
i	4.32	74.0	CH_2	
i'	4.46	74.0	CH_2	

b	5.07	120.7	CH	4.13
o	5.08	117.1	CH ₂	
o'	5.26	117.1	CH ₂	1.11
e	5.44	136.9	CH	
c	5.58	136.8	CH	3.82
g	5.76	117.1	CH	
n	5.90	134.8	CH	
f	---	130.8	Q	
h	---	149.1	Q	

8-[(Benzyloxy)methyl]-1,3,3a,6-tetrahydrocycloocta[c]furan

¹H-NMR (500 MHz, CDCl₃) δ 7.36-7.29 (m, 5H), 5.99 (s, 1H), 5.76-5.73 (m, 1H), 5.59 (t, J = 7.7 Hz, 1H), 5.34 (d, J = 8.2 Hz, 1H), 4.52 (d, J = 11.8 Hz, 1H), 4.47 (d, J = 12.2 Hz, 1H), 4.42 (d, J = 13.1 Hz, 1H), 4.35 (d, J = 13.1 Hz, 1H), 4.10 (d, J = 12.2, 1H), 4.07 (dd, J = 6.8, 7.0 Hz, 1H), 4.01 (d, J = 12.2 Hz, 1H), 3.85 (dd, J = 4.1, 8.6 Hz, 1H), 3.39 (s, br, 1H), 2.83-2.75 (m, 2H); ¹³C-NMR (75 MHz, CDCl₃) δ 142.1, 139.1, 138.3, 129.5, 128.4, 127.8, 127.6, 127.4, 124.0, 117.9, 76.0, 73.0, 71.8, 71.4, 43.1, 27.2; IR (thin film) 2956.3, 2925.0, 1745.0, 1455.9, 1377.8, 1072.3, 1028.6, 930.7, 733.3, 696.7 cm⁻¹; MS-HREI Calcd for C₁₈H₂₀O₂ (M+Li⁺) m/e 275.1623, measured m/e 275.1620.

Assignment of ¹H and ¹³C chemical shifts and NOE correlations

Carbon #	¹ H-Shift	¹³ C- Shift	Type	NOE
d, d'	2.83	27.3	CH ₂	5.75, 5.58
a	3.41	43.1	CH	5.38, 4.08, 3.85
j	3.86	76.1	CH ₂	5.38, 4.39, 4.06, 3.37
k	4.02	73.0	CH ₂	6.00, 5.58, 4.50
j'	4.08	76.1	CH ₂	3.85, 3.37, 6.00
k'	4.12	73.0	CH ₂	6.00, 5.58, 4.50
i	4.37	71.2	CH ₂	6.00, 3.86
i'	4.40	71.2	CH ₂	6.00
l	4.51	71.9	CH ₂	4.11, 4.02, 7.35
l'	4.58	71.9	CH ₂	4.11, 4.02, 7.35
b	5.40	129.5	CH	5.75, 3.86, 3.40
e	5.59	124.1	CH	4.11, 4.02, 2.81

c	5.75	127.4	CH	5.37, 2.78
g	6.00	117.9	CH	4.38, 4.11, 4.02
Ph	7.31	127.7	CH	
Ph	7.35	128.1	CH	4.51
Ph	7.35	127.8	CH	
f	---	138.3	Q	
Ph	---	139.1	Q	
<u>h</u>	---	142.1	Q	

7-[(Benzyloxy)methyl]-1,3,3a,6-tetrahydrocycloocta[c]furan

^1H -NMR (600 MHz, CDCl_3) δ 7.22-7.13 (m, 5H), 6.00 (s, 1H), 5.80 (s, 1H), 5.63 (ddd, $J = 3.1$, 10.1, 13.5, 1H), 5.23 (d, $J = 10.8$ Hz, 1H), 4.34 (s, 2H), 4.22 (d, $J = 5.4$ Hz, 2H), 3.99 (t, $J = 8.1$ Hz, 1H), 3.86 (s, 2H), 3.66 (dd, $J = 5.4$, 9.0 Hz, 1H), 3.34 (s, br, 1H), 2.75 (d, $J = 6.6$ Hz, 2H); ^{13}C -NMR (150 MHz, CDCl_3) δ 142.0, 138.3, 136.9, 128.6, 128.4, 127.8, 127.6, 127.1, 125.6, 117.5, 75.8, 74.3, 72.0, 71.7, 42.9, 28.3; IR (thin film) 2956.3, 2925.0, 1745.0, 1455.9, 1377.8, 1072.3, 1028.6, 930.7, 733.3, 696.7 2956.3, 2925.0, 1745.0, 1455.9, 1377.8, 1072.3, 1028.6, 930.7, 733.3, 696.7 2956.3, 2925.0, 1745.0, 1455.9, 1377.8, 1072.3, 1028.6, 930.7, 733.3, 696.7 cm^{-1} ; MS-HREI Calcd for $\text{C}_{18}\text{H}_{20}\text{O}_2$ (M^+) m/e 275.1623, measured m/e 275.1620.

Assignment of ^1H and ^{13}C chemical shifts and NOE correlations

Carbon #	^1H -Shift	^{13}C - Shift	Type	NOE correlations
d, d'	2.75	27.8	CH_2	5.21, 3.87, 3.35
a	3.34	42.6		4.01, 2.74
j	3.65	75.4	CH_2	5.24, 4.02
k	3.85	74.0	CH_2	6.02, 2.74, 4.33
j'	3.98	75.5	CH_2	3.66, 3.34
i i'	4.22	71.6	CH_2	5.82
l	4.33	71.3	CH_2	3.87, 7.23
b	5.22	128.3	CH	5.66, 3.66
c	5.64	126.9	CH	5.21, 2.73
g	5.79	117.2	CH	4.21, 6.00
f	5.99	125.2	CH	3.85, 5.82
Ph	7.15	127.3	CH	---
Ph	7.20	127.6	CH	4.33
Ph	7.20	128.0	CH	4.33
e		136.9	Q	---
Ph		138.3	Q	---
h		142.0	Q	---

Preparation of Dienynes:

1-Prop-2-ynoxy-hexa-2,4-diene (1).

To a stirring suspension of NaH (1.89 g, 95% dry, 75 mmol) in 100 mL THF at 0 °C, 5.6 mL (50 mmol) of 2,4-hexadien-1-ol were slowly added. . After 15 minutes at 0 °C propargyl bromide (8.3 mL, 80% (w/w) solution in toluene, 75 mmol) was slowly added. . The reaction was left to stir overnight during which time it warmed to room temperature. . The reaction was quenched with 50 mL of saturated NH₄Cl solution and the layers were separated. . The aqueous phase was extracted twice with 50 mL of Et₂O, and the combined organic extracts were washed once with 50 mL of saturated brine solution. . The ethereal solution was dried (MgSO₄), concentrated, purified by flash chromatography (5% EtOAc in Hex). . 5.46 g of the desired diyne were collected as a yellow liquid (74% yield). . Spectral data is consistent with that previously reported.^{2a}

¹H-NMR (300 MHz, CDCl₃) δ 6.23 (dd, J = 10.4 Hz, 15.2 Hz, 1H), 6.05 (dd, J = 15.0, 15.0 Hz, 1H), 5.72 (dq, J = 14.9, 6.7 Hz, 1H), 5.59 (dt, J = 15.3, 6.5 Hz, 1H), 4.12 (s, 2H), 4.07 (d, J = 6.6 Hz, 2H), 2.41 (s, 1H), 1.75 (d, J = 6.6 Hz, 3H); ¹³C-NMR (75 MHz, CDCl₃) δ 134.2, 130.6, 130.5, 125.5, 74.3, 70.0, 56.7, 18.1; IR (FT-IR, film) ν = 3296 ; 3021; 2854; 1114; 1060; 989; 668 cm⁻¹; LREI m/z (%) = [M + H]⁺ 136 (9); HREI Calculated for C₉H₁₂O: 136.0888; Found: 136.0887.

Synthesis of Compound 4

1-*t*-Butyldimethylsiloxy-4-bromo-2-butene

Methyl-4-bromo-crotonate (8.5 mL, 72 mmol) was added to a flask containing 40-mL of dry CH₂Cl₂ under N₂. . The solution was cooled to -78° C, and 180 mL of a 1.0 M solution of DIBAL

(180 mmol) were added very slowly. . The reaction turned from clear to yellow during the addition and returned to clear afterwards. . After stirring for 30 minutes at -78° C the reaction was warmed to 0 °C, and was slowly quenched with saturated Na₂CO₃ (100 mL). . The Li-Al sludge was removed by filtration through Celite. . The layers were separated in a separatory funnel, the organic phase was dried (MgSO₄), and the solvent was removed by evaporation. . The crude alcohol was dissolved in 100 mL of fresh CH₂Cl₂, and diisopropylethylamine (14.1 mL, 79 mmol) was added under N₂. . TBDMS-OTf (18.1 mL, 79 mmol) was then added at 0 °C, and the reaction was left to stir overnight during which time it warmed to room temperature. . The reaction was worked up by flash chromatography though a small plug of silica (4" x 3" dia., 5% EtOAc in Hex). . Evaporation of the solvent yielded 17.13 g (90% yield) of pure product.

¹H-NMR (300 MHz, CDCl₃) δ 5.89-5.87 (m, 2H), 4.21 (dd, J= 2.3, 1.24 Hz, 2H), 4.10-4.08 (m, 1H), 3.99 (d, J = 5.8 Hz, 1H), 0.92 (s, 9H); 0.08 (s, 6H); ¹³C-NMR (75 MHz, CDCl₃) δ 134.7, 125.8, 62.6, 32.4, 25.9, 18.4, -5.3; IR (thin film) 3064.01, 3027.9, 2952.4, 2883.7, 2823.0, 2792.8, 2768.6, 2175.0, 2063.3, 1931.1, 1868.8, 1810.5, 1740.2, 1700.0, 1653.4, 1604.4, 1495.2, 1469.9, 1453.6, 1420.9, 1381.9, 1319.0, 1250.5, 1216.5, 1149.0, 1110.5, 1032.7, 918.7, 844.2, 759.3, 699.8, 650.8, 620.6 cm⁻¹; MS-HREI Calculated for C₆H₁₂BrOSi (M - *t*-Bu⁺) m/e 208.9826, measured m/e 208.9820.

1-(*t*-Butyldimethylsiloxy)-5-oxo-octa-2-en-7-yne

To a suspension of NaH (60% disp. in mineral oil, 3.09 g, 77.4 mmol) in 200 mL dry THF at 0 °C, propargyl alcohol (4.1 mL, 70.9 mmol) was slowly added. . After 15 minutes, 1-bromo-4-(*t*-butyldimethylsiloxy)-2-butene was added as a solution in 50 mL dry THF dropwise via an addition funnel. . After stirring for 3 hours at room temperature, the reaction was refluxed overnight. . The next morning, the reaction was cooled and filtered through Celite to remove the solid NaBr that was suspended in the reaction mixture. . Flash chromatography (5% EtOAc in hexanes) afforded 8.26 g (53% yield) of pure product.

¹H-NMR (300 MHz, CDCl₃) δ 5.82-5.79 (m, 2H), 4.18 (d, J = 1.4 Hz, 2H), 4.14 (d, J = 2.5 Hz, 2H), 4.07 (d, J = 4.7 Hz, 2H), 2.41 (d, J = 2.2 Hz, 2H), 0.90 (s, 9H), 0.06 (s, 6H); ¹³C-NMR (75 MHz, CDCl₃) δ 133.5, 125.2, 79.7, 74.3, 69.7, 63.0, 56.9, 25.9, 18.4, -5.3; IR (thin film) 3311.7,

2955.7, 2930.1, 2886.2, 2857.2, 2739.21, 2117.1, 1676.4, 1472.0, 1463.5, 1389.0, 1376.6, 1360.9, 1255.1, 1104.9, 1958.1, 1006.3, 970.6, 938.8, 922.2, 837.4, 777.0, 725.7, 665.2, 626.9, 480.5 cm^{-1} ; MS-HRFAB Calculated for $\text{C}_{13}\text{H}_{24}\text{O}_2\text{SiLi}$ ($\text{M}+\text{Li}^+$) m/e 247.1706, measured m/e 247.1702.

(2E)-4-(Prop-2-ynyloxy)but-2-enal

1-*t*-butyldimethylsiloxy-5-oxo-octa-2-en-7-yne (8.25 g, 34.3 mmol) was stirred in a dry 50-ml flask under an atmosphere of N_2 . . 38 mL of a TBAF solution (1.0 M in THF, 38 mmol) was added to the silane at room temperature. . After 2 hours, the reaction was poured into a separatory funnel containing 50 mL of 1 N HCl. . The layers were separated and the aqueous layer was washed three times with 50 mL of Et_2O . . The organic extracts were combined, dried (MgSO_4), and purified by flash chromatography (gradient 10, 30, 50% EtOAc in hexanes). . 3.93 g (91% yield) of pure alcohol were collected. . This alcohol (31 mmol) was dissolved in 200 mL of CH_2Cl_2 . . MnO_2 (67.6 g, 778 mmol) was added to the yellow solution to create a stirring black suspension. . The reaction was left to stirring overnight with an overhead stirrer and was not kept under a N_2 atmosphere. . The next morning, the reaction was filtered through Celite, and the solvent was removed under reduced pressure to yield 2.23 (78%) g of pure aldehyde as a yellow liquid.

^1H -NMR (300 MHz, CDCl_3) δ 9.49 (d, J = 7.7 Hz, 1H), 6.77 (dt, J = 16.6, 4.2 Hz, 1H), 6.25 (ddt, J = 15.7, 8.0, 1.5 Hz, 1H), 4.27 (dd, J = 4.1, 1.9 Hz, 2H), 4.15 (d, J = 2.5 Hz, 2H), 2.44 (t, J = 2.5 Hz, 1H); ^{13}C -NMR (75 MHz, CDCl_3) δ 136.4, 134.5, 129.2, 118.3, 79.9, 74.7, 69.9, 57.3; IR (thin film) 3298.7, 3086.9, 3043.1, 3013.7, 2926.8, 2852.9, 2116.5, 1818.5, 1657.5, 1604.3, 1479.2, 1434.8, 1379.2, 1434.8, 1355.9, 1301.6, 1355.9, 1301.6, 1260.0, 1176.0, 1092.9, 1108.0, 1080.1, 1005.7, 954.4, 907.2, 832.5, 746.0, 697.4, 672.0, 636.1, 541.7, 511.3, 422.4 cm^{-1} ; MS-HREI Calculated for $\text{C}_7\text{H}_8\text{O}_2$ (M^+) m/e 124.0524, measured m/e 124.0527.

(2E)-Penta-2,4-dienyl prop-2-ynyl ether (4).

To a stirring white suspension of methyl triphenyl phosphonium bromide (10.86 g, 30.4 mmol) at 0 °C, butyllithium (20.0 mL, 1.6 M solution in Hexanes, 31.9 mmol) was added very slowly over 15 minutes. . The resultant orange solution was stirred for 15 minutes at 0° C prior to the addition of (2*E*)-4-(prop-2-ynyloxy)but-2-enal (1.842 g, 15.2 mmol). . After 3 hours, the reaction had warmed to room temperature. . The reaction was quenched with 50 mL of a saturated brine solution, the layers were separated, and the aqueous phase was washed twice with 50 mL of Et₂O. . The organic layers were combined, dried (MgSO₄), and concentrated. . Flash chromatography (5% EtOAc in hexanes) afforded 0.591 g (32% yield) of pure dienyne as a clear liquid.

¹H-NMR (300 MHz, CDCl₃) δ 6.38-6.28 (m, 2H), 5.76 (dt, J = 13.7, 5.5 Hz, 1H), 5.23 (d, J = 17.0 Hz, 1H), 5.12 (d, J = 10.1 Hz, 1H), 4.15 (d, J = 2.2 Hz, 2H), 4.11 (d, J = 5.8 Hz, 2H), 2.44 (t, J = 2.5 Hz, 1H); ¹³C-NMR (75 MHz, CDCl₃) δ 136.4, 134.5, 129.2, 118.3, 79.9, 74.7, 69.9, 57.3; IR (thin film) 3298.7, 3086.9, 3043.1, 3013.7, 2926.8, 2852.9, 2116.5, 1818.5, 1657.5, 1604.3, 1479.2, 1434.8, 1379.2, 1434.8, 1355.9, 1301.6, 1355.9, 1301.6, 1260.0, 1176.0, 1092.9, 1108.0, 1080.1, 1005.7, 954.4, 907.2, 832.5, 746.0, 697.4, 672.0, 636.1, 541.7, 511.3, 422.4 cm⁻¹; MS-HREI Calculated for C₈H₁₀O (M⁺) m/e 122.0732; measured m/e 122.0728.

Synthesis of Compound (7).

N-Prop-2-ynetolunesulfonamide

Tosyl chloride (10.49 g, 55 mmol) was slowly added as a solution in 20 mL dry THF to a solution of propargylamine (3.4 mL, 50 mmol) and diisopropylethylamine (9.6 mL, 55 mmol) in 100 mL dry THF at room temperature via cannulae and was left to stir overnight. . The next day the reaction mixture was extracted once with saturated NH₄Cl, and once with brine. . The organic extract was dried (MgSO₄) and concentrated. . Flash chromatography (20% EtOAc in hexanes) yielded 9.01 g (86%) of the pure tosyl amide as a white powder. . Spectral data is consistent with that previously reported.¹⁸

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 2.10 (t, 1H, 2.5 Hz), 2.43 (s, 3H), 3.82 (m, 2H), 5.04 (s, br, 1H), 7.31 (d, 2H, $J = 8.5$ Hz), 7.78 (d, 2H, $J = 8.5$ Hz); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ 15.6, 33.1, 66.1, 127.6, 129.9, 136.7, 144.0; MS-HREI Calcd for $\text{C}_{10}\text{H}_{11}\text{NO}_2$ (M^+) m/e 209.0536, measured m/e 209.0572.

N-Hexa-2,4-dienyl-4-methyl-N-prop-2-ynyl-benzenesulfonamide (7)

N-Tosylpropargylamine (0.90 g, 4.3 mmol) and triphenylphosphine (1.13 g, 4.3 mmol) were dissolved in 50 mL dry THF. 2,4-hexadien-1-ol (0.42 g, 4.3 mmol) was added under N_2 . Finally, DIAD (0.85 mL, 4.3 mmol) was added, and the reaction was stirred for five hours. After concentration, flash chromatography (10% EtOAc in hexanes) yielded 1.11 g (85%) of pure dienyne as a white solid.

$^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 7.69 (d, $J = 8.3$ Hz, 2H), 7.26 (d, $J = 8.6$ Hz, 2H), 6.14 (dd, $J = 10.4, 15.0$, 1H), 5.98 (dd, $J = 15.0, 15.0$, 1H), 5.68 (dq, $J = 14.8, 6.8$ Hz, 1H), 5.37 (dt, $J = 14.8, 7.3$ Hz, 1H), 4.04 (d, $J = 1.5$ Hz, 2H), 3.79 (d, $J = 7.1$ Hz, 2H), 2.39 (s, 3H), 1.98-1.97 (t, $J = 1.5$ Hz, 1H), 1.73 (d, $J = 6.9$ Hz, 3H); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ 18.3, 21.8, 35.9, 48.5, 74.0, 76.8, 123.5, 128.0, 129.7, 130.6, 131.2, 135.8, 136.3, 143.8; IR (thin film) 3291, 3282, 3023, 2916, 1348, 1161, 661; MS-HREI Calculated for $\text{C}_{16}\text{H}_{19}\text{NO}_2\text{S}$ (M^+) m/e 289.1136, measured m/e 289.1141.

6-Prop-2-ynyloxy-hexa-1,3-diene (9).

To a stirring suspension of NaH (0.826 g, 95% disp. in mineral oil, 33 mmol) in 100 mL THF at 0°C , 3,5-Hexadien-1-ol (2.668 g, 27 mmol) was slowly added. After stirring for 30 minutes at 0°C , propargyl bromide (2.7 mL, 80 wt. % solution in toluene, 30 mmol) was slowly added to the yellow cloudy reaction, and it was slowly warmed to room temperature. After 1 hour at room temperature, the reaction was warmed to reflux for 5 hours. The reaction was cooled and quenched with 50 mL of saturated brine solution. The layers were separated, and the aqueous phase was extracted twice with 50 mL Et_2O . The combined organic phases were dried

(MgSO₄), and concentrated. . Flash chromatography (5% EtOAc in hexanes) afforded 1.96 g (53% yield) of pure product as a yellow liquid.

¹H-NMR (300 MHz, CDCl₃) δ 6.32 (dt, J = 16.8, 10.3 Hz, 1H), 6.13 (dd, J = 17.4, 15.1 Hz, 1H), 5.71 (ddd, J = 10.9, 10.9, 7.1 Hz, 1H), 5.12 (d, J = 16.6 Hz, 1H), 5.00 (d, J = 10.0 Hz, 1H), 4.16 (d, J = 2.4 Hz, 2H), 3.59 (t, J = 6.8 Hz, 2H), 2.43-2.05 (m, 3H); ¹³C-NMR (75 MHz, CDCl₃) δ 137.2, 133.1, 131.1, 115.9, 80.0, 74.6, 69.6, 58.3, 33.0; IR (thin film) 3298.7, 3086.7, 3011.6, 2973.8, 2939.9, 2896.6, 2857.9, 2216.2, 2116.4, 1803.4, 1738.0, 1653.4, 1603.7, 1476.6, 1442.6, 1418.0, 1373.5, 1357.5, 1243.2, 1165.6, 1104.1, 1047.0, 1005.8, 952.1, 903.2, 846.3, 787.2, 669.5, 635.9, 465.6 cm⁻¹; MS-HREI Calculated for C₉H₁₂O (M⁺) m/e 136.0882, measured m/e 136.0883.

Synthesis of 11

(2E, 4E) Ethyl 2-methyl-2,4-hexadienoate

To a clean, dry 100 mL round bottom flask equipped with a stir bar was added (carbethoxyethylidene)triphenylphosphorane (12.50 g, 0.034 mol). . The flask was sealed under N₂ and 21 mL of CH₂Cl₂ was added to the flask while stirring at room temperature. . Crotonaldehyde (2.50 mL, 0.042 mol) was added drop wise over approximately 10 minutes and the flask was fitted with a reflux condenser and placed in an oil bath at 60 °C and refluxed for 3 ½ hours. . The flask was then removed from the oil bath and concentrated to half its original volume. . To the flask was then added petroleum ether (47 mL) and the solution was filtered to remove the triphenylphosphine oxide which separated from the solution. . The solid was washed with additional petroleum ether (20 mL) and the solution was once again concentrated. . Flash chromatography (10% EtOAc in hexanes) afforded 3.42 g (53% yield) of the unsaturated ester as a colorless liquid. . ¹H NMR (300 MHz, CDCl₃) δ 7.15 (d, J = 11.2 Hz, 1H), δ 6.36 (dd, J = 14.2, 11.8 Hz, 1H), δ 6.08 (dq, J = 14.5, 7.1 Hz, 1H), δ 4.20 (q, J = 7.1 Hz, 2H), δ 1.92 (s, 3H), δ 1.86 (d, J = 6.6 Hz, 3H), δ 1.30 (t, J = 7.1 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 168.2, 138.1, 137.2, 127.1, 124.6, 60.2, 18.7, 14.2, 12.4;

(2E, 4E)-2-Methyl-2, 4-hexdien-1-ol

In a 250 mL round bottom flask equipped with a stir bar a suspension of LiAlH_4 (2.20 g, 0.058 mol) in 80 mL of Et_2O was stirred at 0°C . A solution of ethanol (2.10 mL, 0.058 mol) in 18 mL of Et_2O was added slowly and H_2 evolution was noted. In a second 250 mL round bottom flask equipped with a stir bar (2E, 4E)-2-methyl-2,4-hexadienoate (3.42 g, 0.022 mol) as a solution in 61 mL of Et_2O was stirred at 0°C . To the unsaturated ester was slowly added 12.2 mL of the, presumably, lithium aluminum monoethoxyhydride solution and the flask was stirred at 0°C for 1 hour. This process was repeated an additional three times until a total of 49 mL of the reagent had been added. The solution was then quenched using a 30% aqueous solution of Rochelle's Salt (potassium sodium tartrate). The resulting suspension was filtered and washed with H_2O and Et_2O before the layers were separated. The aqueous phase was extracted three times with 25 mL of Et_2O . The organic layers were combined, dried (Na_2SO_4) and concentrated to afford 2.29 g (92% yield) of the unsaturated alcohol. ^1H NMR (300 MHz, CDCl_3) δ 6.25 (dd, $J = 13.2$, 11.2 Hz, 1H), δ 5.98 (d, $J = 10.9$ Hz, 1H), δ 5.63 (dq, $J = 14.5$, 6.6 Hz, 1H), δ 3.99 (s, 2H), δ 2.80 (broad s, 1H), δ 1.78 (d, $J = 7.1$ Hz, 3H), δ 1.74 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 134.5, 129.5, 127.4, 125.2, 68.7, 18.7, 14.3.

(2E, 4E)-1-(Prop-2-ynoxy)-2-methyl-hexa-2,4-diene (11).

In a 250 mL round bottom flask equipped with a stir bar a suspension of NaH (0.92g, 60% dispersion in mineral oil, 22.8 mmol) in 38 mL of THF was stirred at 0°C . 2-Methyl-2,4-hexadien-1-ol (2.29 g, 20.4 mmol) was added over 5 minutes. After 45 minutes propargyl bromide (2.39 mL, 80% wt. solution in toluene, 21.4 mmol) was added and the reaction was stirred overnight during which time it slowly warmed to room temperature. Ice water (40 mL) was added to quench the reaction and the layers were separated. The aqueous phase was washed two times with 50 mL of Et_2O . The organic layers were combined, dried (Na_2SO_4) and concentrated. Flash chromatography (10 % EtOAc in hexanes) afforded 1.22 g (67 % yield) of pure diene-yne as a yellow liquid. ^1H NMR (300 MHz, CDCl_3) δ 6.27 (dd, $J = 13.1$, 10.9 Hz, 1H), δ 6.02 (d, $J = 10.9$ Hz, 1H), δ 5.71 (dq, $J = 14.8$, 6.5 Hz, 1H), δ 4.08 (d, $J = 2.1$ Hz, 2H), δ

3.98 (s, 2H), δ 2.41 (t, J = 2.1 Hz, 1H), δ 1.78 (d, J = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 131.0, 130.3, 128.4, 127.3, 80.1, 75.6, 74.4, 56.6, 18.6, 14.5; MS-HREI Calculated for $\text{C}_{10}\text{H}_{14}\text{O}$ ($\text{M}-\text{CH}_3$) m/e 135.1011, measured m/e 135.1013 and 135.1006.

Synthesis of Compound 13.

(2E, 4E) Ethyl-3-Methyl-2,4-hexadienoate/(2E, 4Z) Ethyl-3-Methyl-2,4-hexadienoate

To a clean, dry 500 mL round bottom flask equipped with a stir bar was added *n*-butyl lithium (32 mL, 2.5 M solution in hexanes, 80.0 mmol). The *n*-BuLi solution was concentrated, dissolved in dry Et_2O (250 mL) and placed in an ice bath to stir at 20 °C.

Ethyltriphenylphosphonium bromide (25.11 g, 67.65 mmol) was added portion wise, slowly over five minutes and the flask was removed from the bath and stirred at room temperature for 1 hour. Ethyl 3-methyl-4-oxobut-2-enoate (9.16 g, 64.5 mmol) as a solution in Et_2O was then added drop wise over 20 minutes via an addition funnel. Once the addition was complete the flask was then left to stir at room temperature overnight (16 hrs.). The solution was filtered, washed with Et_2O and the layers were separated. The organic layer was washed three times with 100 mL of H_2O , dried (Na_2SO_4) and concentrated to afford 5.51 g (55% yield) of the unsaturated ester as a brown liquid in a 2:1 mixture of the 2E, 4Z and 2E, 4E double bond isomers. Spectral properties matched those previously reported for these compounds. ^1H NMR (300 MHz, CDCl_3) (2E,4E) δ 6.20-6.0(m, 2H), δ 5.8-5.6 (m, 1H), δ 4.10 (q, J = 7.0 Hz, 2H), δ 2.22 (s, 3H), δ 1.8 (dd, J = 6.9 Hz, 1.5 Hz, 1H), δ 1.22 (t, J = 7.0 Hz, 3H); (2E,4Z) δ 5.86 (d, J = 12.1 Hz, 1H), δ 5.8-5.6 (m, 2H), δ 4.11 (q, J = 7.0 Hz, 2H), δ 2.22 (s, 3H), δ 1.80 (dd, J = 6.9 Hz, 1.5 Hz, 1H), δ 1.23 (t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 166.9, 166.6, 152.8, 152.2, 134.7, 132.5, 131.8, 129.2, 118.1, 117.2, 63.4, 59.5, 30.7, 19.1, 18.5, 15.0, 14.3, 13.7.

(2E, 4E)-3-Methyl-2,4-hexadienoic acid/(2Z, 4E)-3-Methyl-2,4-hexadienoic acid

In a clean, dry 250 mL round bottom flask equipped with a stir bar a solution of ethyl 3-methylhexa-2,4-dienoate (5.00 g, 32.4 mmol) in Et₂O (30 mL) was stirred at 0 °C. . In an addition funnel a solution of potassium hydroxide (5.15 g, 91.8 mmol) in absolute ethanol (120 mL) was prepared and added to the flask drop wise over 30 minutes. . The flask was then transferred to an oil bath and stirred at 55 °C for 2 hours before being removed and stirred at room temperature overnight (16 hrs.). . The solution was partially concentrated, poured into H₂O (150 mL) and the layers were separated. . The aqueous layer was washed four times with 25 mL of Et₂O before being acidified. . The aqueous layer was then extracted four times with 25 mL of ethyl acetate. . The organic layers were combined, dried (Na₂SO₄) and concentrated to afford 3.17 g (77% yield) of the unsaturated acid as a yellow liquid in the same ratio of double bond isomers as the ester. . ¹H NMR (300 MHz, CDCl₃) δ 6.20-6.10 (m, 2H), δ 5.91 (d, J = 11.8 Hz, 2H), δ 5.80-5.60 (m, 4H), δ 2.28 (s, 3H), δ 2.27 (s, 3H), δ 1.86 (d, J = 6.8 Hz, 3H), δ 1.85 (d, J = 7.1 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 172.9, 172.5, 155.8, 155.0, 134.7, 133.1, 132.5, 130.2, 117.6, 116.7, 19.5, 18.6, 15.2, 14.0.

(2E, 4E)-3-Methyl-2,4-hexadienoic acid

In a 100 mL round bottom flask equipped with a stir bar a solution of 3-methyl-2,4-hexadienoic acid (0.250 g, 1.99 mmol) in Et₂O (20 mL) was stirred at room temperature. . In a second flask a solution of iodine (6.0 mgs, 0.024 mmol) in benzene (2 mL) was prepared. . The iodine solution was added to the original solution and the flask was equipped with a reflux condenser and stirred under N₂ while being illuminated by a standard 100 W light bulb at 32 cm. for 1 hour. . The resulting solution was washed with aqueous sodium thiosulfate and brine before being dried (Na₂SO₄) and concentrated. . Flash chromatography (10% ethyl acetate in hexanes) afforded 193.4 mgs (77% yield) of the unsaturated acid as a white crystalline solid in the (2E, 4E) isomeric form only. .

¹H NMR (300 MHz, CDCl₃) δ 6.25-6.10 (m, 2H), δ 5.69 (s, 1H), δ 2.27 (s, 3H), δ 1.86 (d, J = 5.2 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 172.2, 155.3, 135.0, 133.4, 116.7, 19.0, 14.3. .

(2E, 4E)-3-Methyl-2,4-hexadien-1-ol

In a clean, dry 100 ml round bottom flask equipped with a stir bar a suspension of LiAlH_4 (269.5 mgs, 7.10 mmol) in 20 mL of Et_2O was stirred at 0°C . (2E, 4E) 3-methyl-2,4-hexadienoic acid (879.5 mgs, 6.98 mmol) as a solution in 10 mL of Et_2O was added slowly. The flask was removed from the bath, warmed to room temperature, and allowed to stir at room temperature for 1 hour. The solution was then cooled to 0°C and quenched with H_2O (10 mL) and 2 M H_2SO_4 (20 mL) and the layers were separated. The aqueous phase was extracted three times with 20 mL of Et_2O . The organic layers were combined, dried (Na_2SO_4) and concentrated. Flash chromatography (20% EtOAc in hexanes) afforded 781.6 mgs (99% yield) of the unsaturated alcohol. ^1H NMR (300 MHz, CDCl_3) δ 6.06 (d, J = 15.1 Hz, 1H), δ 5.70 (dq, J = 15.1 Hz, 6.6 Hz 1H), δ 5.52 (t, J = 6.8 Hz, 1H), δ 4.24 (d, J = 6.8 Hz, 2H), δ 1.77 (d, J = 6.6 Hz, 3H), δ 1.76 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 136.6, 135.3, 127.5, 125.2, 59.6, 18.6, 12.9.

(2E, 4E)-1-(Prop-2-ynoxy)-3-methyl-hexa-2,4-diene (13)

In a clean, dry 100 mL round bottom flask equipped with a stir bar a suspension of NaH (0.300 g, 60% dispersion in mineral oil, 7.51 mmol) in 20 mL of THF was stirred at 0°C . 3-Methyl-2,4 hexadien-1-ol (2.29 g, 20.4 mmol) was added over 5 minutes. After 45 minutes propargyl bromide (0.78 mL, 80% wt. soln. in toluene, 7.00 mmol) was added and the reaction was stirred overnight during which time it slowly warmed to room temperature. Ice water (25 mL) was added to quench the reaction and the layers were separated. The aqueous phase was washed three times with 25 mL of Et_2O . The organic layers were combined, dried (Na_2SO_4) and concentrated. Flash chromatography (10 %-20% EtOAc in hexanes) afforded 520.1 mgs (56 % yield) of pure dieneyne as a yellow liquid. ^1H NMR (300 MHz, CDCl_3) δ 6.07 (d, J = 15.6 Hz, 1H), δ 5.70 (dq, J = 15.4, 6.6 Hz, 1H), δ 5.45 (t, J = 6.8 Hz, 1H), δ 4.18 (d, J = 6.8 Hz, 2H), δ 4.12 (d, J = 2.2 Hz, 2H), δ 2.42 (t, J = 2.2 Hz, 1H), δ 1.78 (s, 3H), δ 1.77 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 138.3, 135.3, 125.2, 124.2, 80.2, 74.5, 66.1, 57.1, 18.6, 13.1; MS-HRES Calculated for $\text{C}_{10}\text{H}_{14}\text{O}$ (M^+Na) m/e 173.0942, measured m/e 173.0939.

Synthesis of Compound 15.

(2E, 4E) Methyl-4-Methyl-2,4-hexadienoate

In a 250 mL round bottom flask equipped with a stir bar a suspension of NaH (3.74 g, 0.156 mol) in 150 mL of benzene was stirred at room temperature. . Trimethyl phosphonoacetate (32.7 mL, 0.202 mol) was then added to the solution drop-wise over 20 minutes. . After 1 hour at room temperature *trans*-2-Methyl-2-butenal (11.5 mL, 0.119 mol) was added and the flask was fitted with a reflux condenser and placed in an oil bath at 65 °C to stir for 30 minutes. . Ice water (100 mL) was added to quench the reaction and the layers were separated. . The aqueous phase was washed three times with 50 mL of hexanes. . The organic layers were combined, dried (Na₂SO₄) and concentrated. . The pure unsaturated ester was recovered in a quantitative yield as a yellowish liquid. . ¹H NMR (300 MHz, CDCl₃) δ 7.32 (d, J = 15.6 Hz, 1H), δ 5.96 (q, J = 7.1 Hz, 1H), δ 5.77 (d, J = 15.6 Hz, 1H), δ 3.72 (s, 3H), δ 1.78 (d, J = 7.1 Hz, 3H), δ 1.74 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 167.5, 149.5, 136.3, 133.5, 114.6, 51.4, 14.6, 11.8.

(2E, 4E)-4-Methyl-2,4-hexadien-1-ol

In a 250 mL round bottom flask equipped with a stir bar a suspension of LiAlH₄ (4.41 g, 0.116 mol) in 160 mL of Et₂O was stirred at 0 °C. . A solution of ethanol (4.2 mL, 0.115 mol) in 36 mL of Et₂O was added slowly and H₂ evolution was noted. . In a second 500 mL round bottom flask equipped with a stir bar (2E, 4E)-4-methyl-2,4-hexadienoate (10.6 g, 0.075 mol) as a solution in 200 mL of Et₂O was stirred at 0 °C. . To the unsaturated ester was then added slowly 40.0 mL of the, presumably, lithium aluminum monoethoxyhydride solution and the flask was stirred at 0 °C for 1 hour. . This process was repeated an additional three times until a total of 160 mL of the reagent had been added. . The solution was then quenched using 30% aqueous solution of Rochelle's Salt (potassium sodium tartrate). . The resulting suspension was filtered and washed with H₂O and Et₂O before the layers were separated. . The aqueous phase was extracted three

times with 25 mL of Et₂O. . The organic layers were combined, dried (Na₂SO₄) and concentrated to afford 5.97 g (71% yield) of the unsaturated alcohol. . ¹H NMR (300 MHz, CDCl₃) δ 6.23 (d, J = 15.3 Hz, 1H), δ 5.69 (dt, J = 15.6 Hz, 6.3 Hz, 1H), δ 5.56 (q, J = 6.8 Hz, 1H), δ 4.16 (d, J = 6.3 Hz, 2H), δ 2.61 (broad s, 1H), δ 1.73 (s, 3H), δ 1.72 (d, J = 6.8 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 136.3, 133.6, 127.1, 124.6, 63.7, 13.8, 12.0.

(2E, 4E)-1-(Prop-2-ynoxy)-4-methyl-hexa-2,4-diene (15).

In a 500 mL round bottom flask equipped with a stir bar a suspension of NaH (1.44g, 60% dispersion in mineral oil, 59.9 mmol) in 96 mL of THF was stirred at 0 °C. . To this solution was added 4-methyl-2,4 hexadien-1-ol (5.97 g, 53.3 mmol) over 5 minutes. . After 45 minutes propargyl bromide (6.23 mL, 80% wt. solution in toluene, 55.9 mmol) was added and the reaction was stirred overnight during which time it slowly warmed to room temperature. . Ice water (50 mL) was added to quench the reaction and the layers were separated. . The aqueous phase was washed three times with 25 mL of Et₂O. . The organic layers were combined, dried (Na₂SO₄) and concentrated. . Flash chromatography (10 % EtOAc in hexanes) afforded 4.28 g (53 % yield) of pure dieneyne as a yellow liquid. . ¹H NMR (300 MHz, CDCl₃) δ 6.28 (d, J = 15.6 Hz, 1H), δ 5.60 (dt, J = 15.6, 6.3 Hz, 1H), δ 5.58 (q, J = 6.1 Hz, 1H), δ 4.13 (d, J = 2.1 Hz, 2H), δ 4.11 (d, J = 6.8 Hz, 2H), δ 2.42 (t, J = 2.1 Hz, 1H), δ 1.73 (s, 3H), δ 1.72 (d, J = 6.3 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 139.0, 133.9, 127.9, 121.3, 79.9, 74.4, 70.7, 56.8, 13.9, 12.0; MS-HRES Calculated for C₁₀H₁₄O (M⁺Na) m/e 173.0942, measured m/e 173.0939.

Synthesis of Compound 17.

(2E)-Methyl-5-methyl-2,4-hexadienoate

To a clean, dry Schlenk tube equipped with a stir bar was added triethylamine (2.70 mL, 18.8 mmol) and the tube was stirred at room temperature. . Methyl acrylate (1.62 mL, 18.8 mmol) was then added along with 1-bromo-2-methylpropene (1.56 mL, 15.0 mmol). . The tube was

stirred vigorously to ensure homogeneity while Pd(OAc)₂ (33.8 mgs, 0.150 mmol) along with triphenylphosphine (79.1 mgs, .301 mmol) were added. . The tube was then put through a freeze-pump-thaw cycle three times, back-filled with nitrogen and placed in an oil bath at 100 °C to stir for four days. . The tube was then removed from the bath and cooled to room temperature before being diluted with Et₂O (30 mL), filtered through Celite, and concentrated. . Flash chromatography (5 % EtOAc in hexanes) afforded 1.45 g (69 % yield) of the unsaturated ester as a colorless liquid. . Spectral properties were consistent with those previously reported. . ¹H NMR (300 MHz, CDCl₃) δ 7.54 (dd, J = 15.1, 11.5 Hz, 1H), δ 5.94 (d, J = 12.1 Hz, 1H), δ 5.74 (d, J = 15.2 Hz, 1H), δ 3.71 (s, 3H), δ 1.85 (overlapping s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 168.2, 146.2, 141.1, 123.6, 117.9, 51.2, 26.4, 18.8.

(2E)-5-Methyl-2,4-hexadien-1-ol

In a 35 ml round bottom flask equipped with a stir bar a suspension of LiAlH₄ (300.7 mgs, 7.92 mmol) in 20 mL of Et₂O was stirred at 0 °C. . (2E)-methyl 5-methyl-2,4-hexadienoate (1.10 g, 7.87 mmol) as a solution in 5 mL of Et₂O was added slowly. . The flask was then removed from the bath, warmed to room temperature, and allowed to stir at room temperature for 45 minutes. . The solution was then cooled to 0 °C and quenched with H₂O (10 mL) and 2 M H₂SO₄ (20 mL) and the layers were separated. The aqueous phase was extracted three times with 50 mL of Et₂O. The organic layers were combined, dried (Na₂SO₄) and concentrated. Flash chromatography (20% EtOAc in hexanes) afforded 791.8 mgs (89% yield) of the unsaturated alcohol. Spectral properties are consistent with those previously reported. ¹H NMR (300 MHz, CDCl₃) δ 6.43 (dd, J = 15.1, 11.0 Hz, 1H), δ 5.94 (d, J = 12.1 Hz, 1H), δ 5.64 (dt, J = 15.2 Hz, 6.4 Hz, 1H), δ 4.11 (d, J = 6.4 Hz, 2H), δ 2.69 (broad s, 1H), δ 1.73 (overlapping s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 135.7, 129.0, 124.2, 63.3, 25.8, 18.1.

(2E)-1-(Prop-2-ynoxy)-5-methyl-hexa-2,4-diene (17).

In a 50 ml round bottom flask equipped with a stir bar a suspension of NaH (142.2 mgs, 5.93 mmol) in 10 mL of THF was stirred at 0 °C. 5-methyl-2,4 hexadien-1-ol (579.4 mgs 5.17 mmol) as a solution in 2 mLs of dry THF was added over 5 minutes. After 45 minutes propargyl

bromide (1.08 mL, 80% wt. solution in toluene, 5.42 mmol) was added and the reaction was stirred overnight during which time it slowly warmed to room temperature. Ice water (40 mL) was added to quench the reaction and the layers were separated. The aqueous phase was washed four times with 25 mL of Et₂O. The organic layers were combined, dried (Na₂SO₄) and concentrated. Flash chromatography (5 % EtOAc in hexanes) afforded 344.3 mgs (44 % yield) of pure diene-yne as a yellow liquid. ¹H NMR (300 MHz, CDCl₃) δ 6.48 (dd, J = 15.1, 10.9 Hz, 1H), δ 5.48 (d, J = 10.9 Hz, 1H), δ 5.60 (dt, J = 15.1 Hz, 6.6 Hz, 1H), δ 4.14 (d, J = 2.1 Hz, 2H), δ 4.10 (d, J = 6.6 Hz, 2H), δ 2.42 (t, J = 2.1 Hz, 1H), δ 1.77 (d, J = 5.2 Hz, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 136.8, 130.8, 125.4, 124.3, 80.1, 74.5, 70.5, 57.0, 26.3, 18.7; MS-HREI Calculated for C₁₀H₁₄O (M⁺) m/e 150.1045, measured m/e 150.1038.

Synthesis of Compound 32.

Ethyl-3,5-hexadienoate

To a stirring solution of diisopropylamine (28.0 g, 0.28 mol) in approximately 400 mL of THF at -78 °C, butyllithium (112 mL, 2.5 M solution in hexanes, 0.28 mol) was slowly added. This yellow solution was stirred at -78 °C for 30 minutes prior to the addition of HMPA (57.5 mL, 0.33 mol). A room temperature solution of ethyl sorbate (35.0 g, 0.25 mol) in 50 mL of THF was slowly added to the yellow solution of LDA via cannulae. The reaction was stirred at -78 °C for 1 hour, and was then poured into 500 mL of 1.4 M acetic acid at 0 °C. The layers were separated and the aqueous phase was extracted twice with 200 mL of pentane. The organic layers were combined, dried (Na₂SO₄), and concentrated. Final purification was achieved by vacuum distillation (b.p. = 45 °C @ 0.7 mm Hg), which yielded 13.75 g (40%) of the desired unconjugated ester. Spectral data was consistent with that previously reported.¹⁸

¹H-NMR (300 MHz, CDCl₃) δ 6.31 (dt, J = 16.8, 10.2 Hz, 1H), 6.12 (dd, J = 15.4, 10.4 Hz, 1H), 5.76 (ddd, J = 14.8, 7.4, 7.4 Hz, 1H), 5.14 (d, J = 16.2 Hz, 1H), 5.03 (d, J = 10.2 Hz, 1H), 4.12 (q, J = 7.1 Hz, 2H), 3.19 (dd, J = 7.4, 1.1 Hz, 2H), 1.24 (t, J = 7.1 Hz, 3H); ¹³C-NMR (75 MHz,

CDCl_3) δ 171.6, 136.5, 134.4, 125.9, 117.1, 61.0, 38.3, 14.6.

3,5-Hexadien-1-ol

Ethyl 3,5 hexadienoate (2.75 g, 20 mmol) was slowly added as a solution in 20 mL anhydrous ether to a suspension of 0.75 g lithium aluminum hydride (20 mmol) in 50 mL of anhydrous ether under N_2 and was left to react overnight. The reaction was quenched with ~450 mL of Rochelle's salt (30% w/w) solution and the layers were separated. The aqueous layer was extracted 3x with 150 mL pentane. The organic extracts were combined, dried (MgSO_4), and concentrated. Flash chromatography (100% CH_2Cl_2) yielded 1.58 g (81%) of the pure alcohol. Spectral data was consistent with that previously reported.¹⁸

^1H -NMR (300 MHz, CDCl_3) δ 1.93 (s, br, 1H), 2.34 (qd, 2H, $J_1 = 6.6$ Hz, $J_2 = 1.1$ Hz), 3.66 (t, 2H, $J = 6.6$ Hz), 5.00 (dt, 1H, $J_1 = 9.6$ Hz, $J_2 = 0.5$ Hz), 5.12 (dt, 1H, $J_1 = 17.6$ Hz, $J_2 = 0.5$ Hz), 5.67 (m, 1H), 6.12 (m, 1H), 6.41 (m, 1H); ^{13}C -NMR (75 MHz, CDCl_3) δ 36.3, 62.2, 116.2, 130.8, 133.9, 137.0.

N-Hexa-3,5-dienyl-4-methyl-N-prop-2-ynyl-benzenesulfonamide (32).

N-tosylpropargylamide (2.23 g, 11 mmol) and triphenylphosphine (2.88 g, 11 mmol) were dissolved in 100 mL dry THF. 3,5-Hexadien-1-ol (1.04 g, 11 mmol) was added. Finally, DIAD (2.2 mL, 11 mmol) was added, and the reaction was stirred for five hours. After concentration, flash chromatography (10% EtOAc in hexanes) yielded 2.19 g (69%) of pure substrate as a clear oil.

^1H -NMR (300 MHz, CDCl_3) δ 7.73 (d, $J = 8.3$ Hz, 2H), 7.30 (d, $J = 8.1$ Hz, 2H), 6.29 (dt, 16.8, 10.3 Hz, 1H), 6.12 (dd, $J = 15.1$, 10.3 Hz, 1H), 5.63 (ddd, $J = 15.1$, 7.3, 7.3 Hz, 1H), 5.14 (d, $J = 16.6$ Hz, 1H), 5.03 (d, $J = 10.0$ Hz, 1H), 4.15 (d, $J = 2.0$ Hz, 2H), 3.27 (t, $J = 7.3$ Hz, 2H), 2.45-2.36 (m, 5H), 2.05 (s, 1H); ^{13}C -NMR (75 MHz, CDCl_3) δ 143.7, 126.9, 136.1, 133.9, 130.4, 129.7, 116.4, 76.2, 74.0, 46.1, 36.7, 31.3, 21.8; IR (thin film) 3291.0, 3085.7, 3037.3, 2980.8, 2924.9, 2870.3, 2586.1, 2306.7, 2119.9, 1919.3, 1805.8, 1733.3, 1652.3, 1598.7, 1494.8, 1453.6, 1400.6, 1348.1, 1306.4, 1274.2, 1241.8, 1163.1, 1120.0, 1092.2, 1048.1, 1006.0, 953.7, 903.0,

845.3, 815.0, 742.8, 703.5, 660.9, 580.2, 546.5, 507.4 cm^{-1} ; MS-HREI Calcd for $\text{C}_{16}\text{H}_{19}\text{NO}_2\text{S}$ (M^+) m/e 289.1137, measured m/e 289.1130.

Synthesis of Compound 35

1-Bromo-2-[2-(methoxymethoxy)ethyl]benzene

To a 100 mL round bottom flask containing 50 mL of THF 2-(2-bromophenyl)ethanol (0.68 mL, 5.0 mmol) was added, and the clear solution was chilled in an ice/water bath. Diisopropylethylamine (1.3 mL, 7.5 mmol) was added, and the reaction remained clear. Chloromethoxymethyl ether (0.42 mL, 5.5 mmol) was added and the reaction was stirred overnight during which time it warmed to room temperature. The reaction was concentrated and placed directly onto a flash chromatography column. Elution with 10% EtOAc in hexanes produced 1.08 g (88% yield) of the pure protected alcohol as a clear, viscous liquid.

^1H -NMR (300 MHz, CDCl_3) δ 7.54 (dd, J = 8.0, 0.8 Hz, 1H), 7.30-7.21 (m, 2H), 7.08 (ddd, J = 7.6, 7.6, 3.0 Hz, 1H), 4.62 (s, 2H), 3.77 (t, J = 7.0 Hz, 2H), 3.30 (s, 3H), 3.05 (t, J = 7.0 Hz, 2H); ^{13}C -NMR (75 MHz, CDCl_3) δ 138.3, 133.0, 131.3, 128.3, 127.6, 124.9, 96.5, 66.8, 55.4, 36.7; IR (thin film) 3429.4, 3057.6, 2825.8, 2727.7, 2324.6, 1923.6, 1594.8, 1568.1, 1472.0, 1441.0, 1317.4, 1161.8, 1028.8, 933.2, 740.0, 657.2 cm^{-1} ; MS-HREI Calculated for $\text{C}_9\text{H}_{10}\text{BrO}$ ($\text{M}^+ - \text{CH}_3\text{OH}$) m/e 212.9915, measured m/e 212.9914.

1-(3-Trimethylsilylprop-2-ynyl)-2-[2-(methoxymethoxy)ethyl]benzene

1-Bromo-2-[2-(methoxymethoxy)ethyl]benzene (1.91 g, 7.81 mmol) was dissolved in 20 mL of THF, and the clear solution was cooled in a dry ice/acetone bath. Butyllithium (5.4 mL, 1.6 M solution in hexanes, 8.59 mmol) was slowly added, and the reaction remained clear. After stirring for 20 minutes at -78°C , MgBr_2 (0.876 g, 4.76 mmol) was slowly added as a solution in 25 mL of THF. Finally, after stirring for 40 minutes at -78°C , propargyl bromide (0.85 mL, 5.18 mmol) was slowly added, causing the reaction to become slightly yellow colored. After 8 hours,

the reaction bath had warmed to 5 °C, and TLC shows no starting material. Pouring the reaction mixture onto a separatory funnel containing 50 mL of saturated NH₄Cl quenched the reaction. A white precipitate formed. The layers were separated, and approximately 15 mL of H₂O was added to the aqueous layer to dissolve the precipitate. The aqueous layer was extracted once with 50 mL of Et₂O, and the combined organic extracts were washed once with 50 mL of saturated brine solution. The organic extracts were combined, concentrated (MgSO₄), and purified by flash chromatography (5% EtOAc in hexanes). 1.93 g (89% yield) of clear, viscous liquid were collected.

¹H-NMR (300 MHz, CDCl₃) δ 7.46-7.20 (m, 4H), 4.61 (s, 2H), 3.76 (t, J = 7.1 Hz, 2H), 3.67 (s, 2H), 3.30 (s, 3H), 2.95 (t, J = 6.9 Hz, 2H), 0.18 (s, 9H); ¹³C-NMR (75 MHz, CDCl₃) δ 136.6, 134.7, 129.6, 128.7, 126.9, 126.7, 104.2, 96.3, 87.0, 67.7, 55.1, 32.8, 24.0, 0.03; IR (thin film) 2955.5, 2930.0, 2885.3, 2727.6, 1471.9, 1463.3, 1437.4, 1379.2, 1361.6, 1281.1, 1204.5, 1151.3, 1120.0, 1057.8, 1006.2, 960.6, 939.4, 836.9, 814.1, 777.8, 730.1, 695.5, 673.2, 664.2 cm⁻¹; MS-HREI Calculated for C₁₅H₂₀OSi (M⁺ – CH₃OH) m/e 244.1283, measured m/e 244.1279.

2-[2-(3-Trimethylsilylprop-2-ynyl)phenyl]ethanol

2.46 g of 1-(3-trimethylsilylprop-2-ynyl)-2-[2-(methoxymethoxy)-ethyl]-benzene (8.90 mmol), was dissolved in 100 mL of dry MeOH in a 250-mL round bottom flask. 5 drops of concentrated (12.1 M) HCl were added and the reaction was warmed to reflux. After 12 hours, 0.2 mL of Et₃N was added to neutralize the acid. The clear solution was concentrated and purified by flash chromatography (20% EtOAc in Hex). 1.83 g (89% yield) of a clear, viscous liquid were collected.

¹H-NMR (300 MHz, CDCl₃) δ 7.47-7.43 (m, 1H), 7.26-7.18 (m, 3H), 3.77 (dd, br, J = 10.7 4.9 Hz, 2H), 3.65 (s, 2H), 2.93 (td, J = 6.6, 0.8 Hz, 2H), 0.16 (s, 9H); ¹³C-NMR (75 MHz, CDCl₃) δ 136.5, 135.2, 130.2, 129.4, 127.4, 127.2, 104.5, 63.2, 36.0, 24.4, 0.3; IR (thin film) 3368.9, 3064.6, 3021.9, 2958.8, 2175.3, 1924.0, 1740.0, 1604.0, 1490.8, 1452.3, 1420.8, 1373.9, 1319.5, 1098.9, 1045.6, 944.2, 884.1, 759.5, 719.9, 699.2, 649.8, 619.9, 585.3, 546.7, 446.9 cm⁻¹; MS-HRESI Calculated for C₁₄H₂₁OSi (MH⁺) m/e 233.1362, measured m/e 233.1358.

2-[2-(3-Trimethylsilylprop-2-ynyl)phenyl]acetaldehyde

Pyridiniumchlorochromate (2.54 g, 12 mmol) was dissolved in 250 mL of CH₂Cl₂. 2-[2-(3-Trimethylsilylprop-2-ynyl)phenyl]ethanol was added with 3 mL of CH₂Cl₂, and the reaction instantly turned from orange to dark brown. It was stirred overnight at room temperature. The next morning, the reaction mix was filtered through celite and silica, concentrated, and purified by flash chromatography (5% EtOAc in hexanes). 1.33 g (73% yield) of the pleasant smelling aldehyde were collected.

¹H-NMR (300 MHz, CDCl₃) δ 9.74 (t, J = 1.9 Hz, 1H), 7.46-7.43 (m, 1H), 7.32-7.29 (m, 2H), 7.28-7.16 (m, 1H), 3.79 (d, J = 1.9 Hz, 2H), 3.56 (s, 2H), 0.15 (s, 9H); ¹³C-NMR (75 MHz, CDCl₃) δ 199.3, 135.9, 131.2, 130.8, 129.8, 128.3, 127.8, 103.7, 87.9, 48.1, 25.0, 0.2; IR (thin film) 3428.0, 3066.4, 3024.3, 2959.9, 2899.5, 2823.0, 2724.6, 2175.2, 1948.7, 1725.0, 1642.7, 1603.4, 1576.0, 1491.0, 1453.7, 1412.0, 1386.2, 1320.2, 1030.4, 1018.5, 937.6, 844.0, 759.7, 759.7, 699.9, 646.7, 619.8, 522.3, 490.2, 445.2, 415.0; MS-HRESI Calculated for C₁₄H₁₉OSi (MH⁺) m/e 231.1205, measured m/e 231.1195.

1-[(2E)-Penta-2,4-dienyl]-2-(3-trimethylsilylprop-2-ynyl)benzene

Allyltriphenylphosphonium bromide (4.41 g, 11.5 mmol) was weighed into a 100 mL round bottom flask and was suspended in 25 mL of THF. The stirring white suspension was cooled in a dry ice/acetonitrile (approximately -40° C) for 15 minutes. Butyllithium (7.9 mL, 1.6 M solution in hexanes, 13 mmol) was slowly added causing the reaction to become red. After 30 minutes at -40° C, 2-[2-(3-trimethylsilylprop-2-ynyl)phenyl]acetaldehyde (1.33 g, 5.77 mmol) was added as a solution in 25 mL THF. The reaction was stirred for 30 minutes at -40° C, and at room temperature for 3 hours. The reaction was quenched with 50 mL of H₂O, and the layers were separated. The aqueous phase was washed twice with Et₂O, and the combined organic phases were washed once with saturated brine. The organic extract was dried (MgSO₄), concentrated, and purified by flash chromatography (1% EtOAc in Hex). 0.37 g (25% yield) of a light yellow liquid were collected. *The NMR spectra are reported for a mixture of two isomers (E/Z ~ 1:1.3).*

^1H -NMR (300 MHz, CDCl_3) δ 7.49-7.15 (m, 8H), 6.78 (ddd, $J = 17.1, 8.4, 11.1$ Hz, 1H), 6.30 (ddd, $J = 16.9, 10.2, 10.1$ Hz, 1H) 6.18-5.97 (m, 2.6 H), 5.86-5.77 (m, 1.3 H), 5.53 (dd, $J = 8.4, 17.0$ Hz, 1H), 5.26 (d, $J = 17.0$ Hz, 1H), 5.20 (d, $J = 10.2$ Hz, 1H), 5.10 (d, $J = 16.0$ Hz, 1.3 H), 5.02 (d, $J = 9.9$ Hz, 1.3H), 3.60-3.46 (m, 4H + (4x1.3)H), 0.15 (s, 9H + (1.3x9)H); ^{13}C -NMR (75 MHz, CDCl_3) δ 137.2, 136.7, 132.2, 131.7, 130.3, 129.6, 129.5, 129.2, 128.4, 127.2, 126.8, 103.7, 87.9, 58.8, 55.7, 25.1, 24.6, 0.2; MS-HREI Calculated for $\text{C}_{17}\text{H}_{22}\text{Si}$ m/e 254.1491, measured m/e 154.1494.

1-[(2*E*)-Penta-2,4-dienyl]-2-prop-2-ynylbenzene (35).

0.671 g (1.4 mmol) of AgNO_2 were weighed into a 50 mL round bottom flask, and MeOH and H_2O were added (1.75 mL and 0.75 mL, respectively) were added to give a cloudy, pale yellow solution. 1-[(2*E*)-Penta-2,4-dienyl]-2-(3-trimethylsilyl-prop-2-ynyl)benzene was added in one portion at room temperature as a solution in 7.5 mL of MeOH. The reaction quickly precipitated a white solid. After stirring for 2 hours, KCN (0.912 g, 14 mmol) was added as a solution in 2 mL of H_2O , and the reaction turned orange. It was stirred for 4 hours, and decanted into a separatory funnel containing 10 mL of a saturated NH_4Cl solution (**CAUTION:** procedure performed in the back of a fume hood). The aqueous phase was extracted twice with Et_2O , and the combined organic extracts were washed once with saturated brine solution. (**CAUTION:** the aqueous phase was slowly mixed with bleach in a fume hood to destroy any cyanide that might have been present. Additionally, all glassware that might have come in contact with the cyanide was carefully rinsed with bleach in a fume hood.) The organic phase was dried (MgSO_4), concentrated, and purified by flash chromatography (1%EtOAc in hexanes). 0.115 g (37% yield) of light yellow liquid was collected. *The NMR spectra are reported for a mixture of two isomers (E/Z ~ 1:1.3).*

^1H -NMR (300 MHz, CDCl_3) δ 7.49-7.15 (m, 8H), 6.77 (ddd, $J = 16.8, 8.4, 11.3$ Hz, 1H), 6.32 (dd, $J = 10.2, 10.2$ Hz, 1H) 6.18-5.97 (m, 2.6 H), 5.86-5.77 (m, 1.3 H), 5.52 (dd, $J = 8.24, 18.1$ Hz, 1H), 5.39 (d, $J = 17.0$ Hz, 1H), 5.20 (d, $J = 10.2$ Hz, 1H), 5.11 (dd, $J = 16.8, 0.8$ Hz, 1.3 H), 5.00 (d, $J = 10.2$ Hz, 1.3H), 3.60-3.46 (m, 4H + (4 x 1.3)H), 2.20-2.18 (m, 1H + 1.3H); ^{13}C -NMR (75 MHz, CDCl_3) δ 137.2, 136.7, 132.2, 131.7, 130.3, 129.6, 129.2, 129.5, 128.4, 127.2, 126.8, 118.3, 115.9 70.8, 35.9, 31.2, 22.6; IR (thin film) 3300.0, 3001.3, 2958.6, 1737.1, 1434.3,

1242.1, 1119.1, 1004.5, 905.8, 844.2, 745.2, 721.2, 696.0, 640.9 cm^{-1} ; MS-HREI Calculated for $\text{C}_{14}\text{H}_{14} (\text{M}^+)$ m/e 182.1096, measured m/e 182.1010.

Part B: ^1H and ^{13}C NMR Spectra for all reported compounds: S38-S100.

¹H-NMR Spectrum of Compound 3

8-[[*(2E,4E)*-Hexa-2,4-dienyloxy]methyl}-6-methyl-1,3,3a,6-tetrahydrocycloocta[*c*]furan

¹³C-NMR Spectrum of Compound 3

8-[[*(2E,4E)*-Hexa-2,4-dienyloxy]methyl]-6-methyl-1,3,3a,6-tetrahydrocycloocta[*c*]furan

COSY-NMR Spectrum of Compound 3

8-[[*(2E,4E)*-Hexa-2,4-dienyloxy]methyl]-6-methyl-1,3,3a,6-tetrahydrocycloocta[*c*]furan

¹H-NMR Spectrum of 1-*t*-Butyldimethylsiloxy-4-bromo-2-butene

^{13}C -NMR Spectrum of 1-*t*-Butyldimethylsiloxy-4-bromo-2-butene

¹H-NMR Spectrum of 1-(*t*-Butyldimethylsiloxy)-5-oxo-octa-2-en-7-yne

^{13}C -NMR Spectrum of 1-(*t*-Butyldimethylsiloxy)-5-oxo-octa-2-en-7-yne

¹H-NMR Spectrum of (2*E*)-4-(Prop-2-ynyloxy)but-2-enal

Figure 4.21. ^{13}C -NMR Spectrum of (2*E*)-4-(Prop-2-ynyloxy)but-2-enal

¹H-NMR Spectrum of Compound 4

(2E)-Penta-2,4-dienyl prop-2-ynyl ether

^{13}C -NMR Spectrum of Compound 4

(2*E*)-Penta-2,4-dienyl prop-2-ynyl ether

¹H-NMR Spectrum of Compound 5

8-Penta-2,4-dienyloxymethyl-1,3,3a,6-tetrahydro-cycloocta[c]furan

¹H-NMR Spectrum of Compound 6

7-Penta-2,4-dienyloxymethyl-1,3,3a,6-tetrahydro-cycloocta[c]furan

¹³C-NMR Spectrum of Compound 6

7-Penta-2,4-dienyloxymethyl-1,3,3a,6-tetrahydro-cycloocta[c]furan

¹H-NMR Spectrum of Compound 7

N-Hexa-2,4-dienyl-4-methyl-N-prop-2-ynyl-benzenesulfonamide

¹³C-NMR Spectrum of Compound 7

N-Hexa-2,4-dienyl-4-methyl-N-prop-2-ynyl-benzenesulfonamide

¹H-NMR Spectrum of Compound 8

N-[(2-Toluenesulfonyl-7-methyl-2,3,7,9a-tetrahydro-1*H*-cycloocta[*c*]pyrrol-5-yl)methyl]-*N*-toluenesulfonyl-hexa-2,4-dien-1-amine

¹³C-NMR Spectrum of Compound 8

N-[(2-Toluenesulfonyl-7-methyl-2,3,7,9a-tetrahydro-1*H*-cycloocta[*c*]pyrrol-5-yl)methyl]-*N*-toluenesulfonyl-hexa-2,4-dien-1-amine

COSY-NMR Spectrum of Compound 8

N-[(2-Toluenesulfonyl-7-methyl-2,3,7,9a-tetrahydro-1*H*-cycloocta[*c*]pyrrol-5-yl)methyl]-*N*-toluenesulfonyl-hexa-2,4-dien-1-amine

(S56)

¹H-NMR Spectrum of Compound 9

6-Prop-2-ynyloxy-hexa-1,3-diene

^{13}C -NMR Spectrum of Compound 9

6-Prop-2-ynyloxy-hexa-1,3-diene

¹H-NMR Spectrum of Compound 10

9-Hexa-3,5-dienyloxymethyl-3,4,4a,7-tetrahydro-1H-cycloocta[c]pyran

¹³C-NMR Spectrum of Compound 10

9-Hexa-3,5-dienyloxymethyl-3,4,4a,7-tetrahydro-1H-cycloocta[c]pyran

¹H-NMR Spectrum of Compound 11

(2E, 4E) Ethyl-3-Methyl-2,4-hexadienoate/(2E, 4Z) Ethyl-3-Methyl-2,4-hexadienoate

^{13}C -NMR Spectrum of Compound 11

(2E, 4E) Ethyl-3-Methyl-2,4-hexadienoate/(2E, 4Z) Ethyl-3-Methyl-2,4-hexadienoate

¹H-NMR Spectrum of Compound 13

(2E, 4E) Ethyl-3-Methyl-2,4-hexadienoate/(2E, 4Z) Ethyl-3-Methyl-2,4-hexadienoate

^{13}C -NMR Spectrum of Compound 13

(2E, 4E) Ethyl-3-Methyl-2,4-hexadienoate/(2E, 4Z) Ethyl-3-Methyl-2,4-hexadienoate

¹H-NMR Spectrum of Compound 14

8{[(2, 4E)-3-Methyl-hexa-2, 4-dienyloxy]methyl} 4, 6-dimethyl-1, 3, 3a, 6-tetrahydrocycloocta[c]furan

¹³C-NMR Spectrum of Compound 14

8{[(2, 4E)-3-Methyl-hexa-2, 4-dienyloxy]methyl} 4, 6-dimethyl-1, 3, 3a, 6-tetrahydrocycloocta[c]furan

¹H-NMR Spectrum of Compound 15

(2E, 4E)-1-(Prop-2-ynyloxy)-4-methyl-hexa-2,4-diene (15).

^{13}C -NMR Spectrum of Compound 15

(2E, 4E)-1-(Prop-2-ynyloxy)-4-methyl-hexa-2,4-diene (15).

¹H-NMR Spectrum of Compound 16

8{[(2E, 4E)-4-Methyl-hexa-2, 4-dienyloxy)methyl} 5, 6-dimethyl-1, 3, 3a, 6-tetrahydrocycloocta[c]furan

¹³C-NMR Spectrum of Compound 16

8{[(2E, 4E)-4-Methyl-hexa-2, 4-dienyloxy]methyl} 5, 6-dimethyl-1, 3, 3a, 6-tetrahydrocycloocta[c]furan

¹H-NMR Spectrum of Compound 17

(2E)-1-(Prop-2-ynyloxy)-5-methyl-hexa-2,4-diene (17).

^{13}C -NMR Spectrum of Compound 17

(2E)-1-(Prop-2-ynoxy)-5-methyl-hexa-2,4-diene (17)

¹H-NMR Spectrum of Compound 20

8-[(Benzyloxy)methyl]-6-methyl-1,3,3a,6-tetrahydrocycloocta[c]furan

¹³C-NMR Spectrum of Compound 20

8-[(Benzyloxy)methyl]-6-methyl-1,3,3a,6-tetrahydrocycloocta[c]furan

Figure 3.31. COSY-NMR Spectrum of Compound 20

8-[(Benzyloxy)methyl]-6-methyl-1,3,3a,6-tetrahydrocycloocta[c]furan

¹H-NMR Spectrum of Compound 22

8-[(Allyloxy)methyl]-6-methyl-1,3,3a,6-tetrahydrocycloocta[c]furan

^{13}C -NMR Spectrum of Compound 22

8-[(Allyloxy)methyl]-6-methyl-1,3,3a,6-tetrahydrocycloocta[c]furan

COSY-NMR Spectrum of Compound 22

8-[(Allyloxy)methyl]-6-methyl-1,3,3a,6-tetrahydrocycloocta[c]furan

NOESY-NMR Spectrum of Compound 22

8-[(Allyloxy)methyl]-6-methyl-1,3,3a,6-tetrahydrocycloocta[c]furan

¹H-NMR Spectrum of Compound 24

8-[(Trimethylsiloxy)methyl]-6-methyl-1,3,3a,6-tetrahydrocycloocta[c]furan

^{13}C -NMR Spectrum of Compound 24

8-[(Trimethylsiloxy)methyl]-6-methyl-1,3,3a,6-tetrahydrocycloocta[c]furan

COSY-NMR Spectrum of Compound 24

8-[(Trimethylsiloxy)methyl]-6-methyl-1,3,3a,6-tetrahydrocycloocta[c]furan

¹H-NMR Spectrum of Compound 26

6-Methyl-8-propyl-1,3,3a,6-tetrahydrocycloocta[c]furan

^{13}C -NMR Spectrum of Compound 26

6-Methyl-8-propyl-1,3,3a,6-tetrahydrocycloocta[c]furan

¹H-NMR Spectrum of Compounds 27 and 28

6-[(Benzyloxy)methyl]-3,4,8,10a-tetrahydro-1H-cycloocta[c]pyran
and 8-Benzyloxymethyl-3,4,4a,7-tetrahydro-1H-cycloocta[c]pyran

¹³C-NMR Spectrum of Compounds 27 and 28

6-[(Benzyloxy)methyl]-3,4,8,10a-tetrahydro-1*H*-cycloocta[*c*]pyran
and 8-Benzyloxymethyl-3,4,4a,7-tetrahydro-1*H*-cycloocta[*c*]pyran

¹H-NMR Spectrum of Compound 29

8-[(Benzyloxy)methyl]-6-methyl-2-tolunesulfonyl-2,3,3a,6-tetrahydro-1*H*-cycloocta[*c*]pyrrole

¹³C-NMR Spectrum of Compound 29

8-[(Benzyloxy)methyl]-6-methyl-2-tolunesulfonyl-2,3,3a,6-tetrahydro-1*H*-cycloocta[*c*]pyrrole

¹H-NMR Spectrum of Compound 31

N-[(2-Tolunesulfonyl-7-methyl-2,3,7,9a-tetrahydro-1*H*-cycloocta[*c*]pyrrol-5-yl)methyl]-*N*-tolunesulfonamide

^{13}C -NMR Spectrum of Compound 31

N-[(2-Tolunesulfonyl-7-methyl-2,3,7,9a-tetrahydro-1*H*-cycloocta[*c*]pyrrol-5-yl)methyl]-*N*-toluenesulfonamide

¹H-NMR Spectrum of Compound 32

N-Hexa-3,5-dienyl-4-methyl-N-prop-2-ynyl-benzenesulfonamide

^{13}C -NMR Spectrum of Compound 32

N-Hexa-3,5-dienyl-4-methyl-N-prop-2-ynyl-benzenesulfonamide

¹H-NMR Spectrum of Compounds 33 and 34

6-(Benzyloxymethyl)-2-toluenesulfonyl-1,2,3,4,8,10a-hexahydrocycloocta[c]pyridine and
8-Benzyloxymethyl-2-(toluene-4-sulfonyl)-1,2,3,4,4a,7-hexahydro-cycloocta[c]pyridine

¹³C-NMR Spectrum of Compounds 33 and 34

6-(Benzyloxymethyl)-2-toluenesulfonyl-1,2,3,4,8,10a-hexahydrocycloocta[c]pyridine and
8-Benzyloxymethyl-2-(toluene-4-sulfonyl)-1,2,3,4,4a,7-hexahydro-cycloocta[c]pyridine

¹H-NMR Spectrum of 1-Bromo-2-[2-(methoxymethoxy)ethyl]benzene

^{13}C -NMR Spectrum of 1-Bromo-2-[2-(methoxymethoxy)ethyl]benzene

¹H-NMR Spectrum of 1-(3-Trimethylsilylprop-2-ynyl)-2-[2-(methoxymethoxy)ethyl]benzene

^{13}C -NMR Spectrum of 1-(3-Trimethylsilylprop-2-ynyl)-2-[2-(methoxymethoxy)ethyl]benzene

¹H-NMR Spectrum of 2-[2-(3-Trimethylsilylprop-2-ynyl)phenyl]ethanol

^{13}C -NMR Spectrum of 2-[2-(3-Trimethylsilylprop-2-ynyl)phenyl]ethanol

¹H-NMR Spectrum of 2-[2-(3-Trimethylsilylprop-2-ynyl)phenyl]acetaldehyde

¹³C-NMR Spectrum of 2-[2-(3-Trimethylsilylprop-2-ynyl)phenyl]acetaldehyde

^1H -NMR Spectrum of 1-[(2*E*)-Penta-2,4-dienyl]-2-(3-trimethylsilylprop-2-ynyl)benzene

^{13}C -NMR Spectrum of 1-[(2*E*)-Penta-2,4-dienyl]-2-(3-trimethylsilylprop-2-ynyl)benzene

¹H-NMR Spectrum of Compound 35

1-[(*E*)-Penta-2,4-dienyl]-2-prop-2-ynylbenzene

^{13}C -NMR Spectrum of Compound 35

1-[(2*E*)-Penta-2,4-dienyl]-2-prop-2-ynylbenzene

¹H-NMR Spectrum of Compounds 36 and 37

10-(Benzyloxymethyl)-8-methyl-5,5a,8,12-tetrahydrocycloocta[b]naphthalene and 9-Benzyloxymethyl-5,5a,8,12-tetrahydro-cycloocta[b]naphthalene

¹³C-NMR Spectrum of Compounds 36 and 37

10-(Benzyloxymethyl)-8-methyl-5,5a,8,12-tetrahydrocycloocta[*b*]naphthalene and 9-Benzyloxymethyl-5,5a,8,12-tetrahydro-cycloocta[*b*]naphthalene

¹H-NMR Spectrum of Compound 39

8[[benzyloxy]methyl] 4, 6-dimethyl-1, 3, 3a, 6-tetrahydrocycloocta[c]furan

^{13}C -NMR Spectrum of Compound 39

8{[benzyloxy]methyl} 4, 6-dimethyl-1, 3, 3a, 6-tetrahydrocycloocta[c]fura

(S110)

¹H-NMR Spectrum of Compound 40

8[[benzyloxy)methyl] 5,6-dimethyl-1, 3, 3a, 6-tetrahydrocycloocta[c]furan

³C-NMR Spectrum of Compound 40

8{[benzyloxy]methyl} 5,6-dimethyl-1, 3, 3a, 6-tetrahydrocycloocta[c]furan

¹H-NMR Spectrum of Compound 43

6-Methyl-1,3,3a,6-tetrahydrocycloocta[c]furan

^{13}C -NMR Spectrum of Compound 43

6-Methyl-1,3,3a,6-tetrahydrocycloocta[c]furan

¹H-NMR Spectrum of Compound 44

4-6-Dimethyl-1,3,3a,6-tetrahydro-cycloocta[c]furan

^{13}C -NMR Spectrum of Compound 44

4-6-Dimethyl-1,3,3a,6-tetrahydro-cycloocta[c]furan

¹H-NMR Spectrum of Compound 45

5-6-Dimethyl-1,3,3a,6-tetrahydro-cycloocta[c]furan

¹³C-NMR Spectrum of Compound 45

5-6-Dimethyl-1,3,3a,6-tetrahydro-cycloocta[c]furan