Supporting Information for:

Gold(I)-Catalyzed Synthesis of Dihydropyrans

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General Information: Unless otherwise noted all commercial materials were used without further purification. Gold(I)-catalyzed reactions used 1,4-dioxane as received from EMD, and were conducted in two dram vials equipped with a magnetic stir bar and fitted with a threaded cap. All other reactions were conducted in flame dried glassware under an inert (N₂) atmosphere with magnetic stirring and dried solvent. Solvents were dried by passage through an activated alumina column under nitrogen. Tris(triphenylphosphinegold)-oxonium tetrafluoroborate ([Ph₃PAu₃O]BF₄) was prepared according to the method of Sharp.¹ (R)-7-phenylhept-3-yn-2-ol was prepared in 81% ee by reduction of the corresponding ynone according to the method of Midland.² Propargyl vinyl ether (**R**)-**5f** was prepared in 96% ee by reduction of the corresponding ynone according to the method of Midland,² and vinylation of the resulting propargyl alcohol according to the method of Yamamoto.³ Vinyl ethers **2**, **5a-j** were prepared from the corresponding propargyl alcohol according to the method of Yamamoto.³ Vinyl ethers **7a-b**, **9a-b**, **11** were prepared by conjugate addition of the corresponding propargyl alkoxide to the requisite ynoate according to the method of Ireland and Wipf, a representative procedure is included below.⁴ Thin-layer chromatography (TLC) analysis of reaction mixtures was performed using Merck silica gel 60 F₂₅₄ TLC plates, and visualized by a combination of UV and permanganate staining. Flash column chromatography was carried out on Merck 60 silica gel (32-63 μm). ¹H and ¹³C NMR spectra were recorded with Bruker DRX-500, AVB-400, AVQ-400, and AV-300 spectrometers and referenced to CDCl₃ unless otherwise noted. IR spectra were recorded on Gemini FTIR and are reported in terms of frequency of absorption (cm⁻¹). Enantiomeric excess was determined on a Shimadzu VP Series Chiral HPLC with detection at 210, 254, and 280 nm. Mass spectral and analytical data were obtained via the Micro-Mass/Analytical Facility operated by the College of Chemistry, University of California, Berkeley.

General Procedure for the Au(I)-Catalyzed Heterocyclization: To a solution of propargyl vinyl ether (1 equiv.) in 1,4-dioxane (0.30 M) was added water (1 equiv.) followed by [Ph₃PAu₃O]BF₄ (1 mol%). The resulting heterogeneous mixture was left to stir at rt, and dissolution of the catalyst was observed within 10 min. The reaction mixture was monitored until TLC analysis indicated consumption of the starting material. The solution was filtered through a silica gel plug (1:1 hexanes:EtOAc), and the filtrate concentrated. The diastereoselectivity was ascertained by ¹H NMR analysis of the crude reaction mixture, and the resulting residue was purified by flash column chromatography to afford the desired pyran product.

Characterization Data for Vinyl Ethers **2, **5a-f**, **i**, **7a-b**, **9a-b**:**

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The crude mixture was purified by flash column chromatography (2% TEA in hexanes eluent) to afford the desired vinyl ether (1.52 g, 70% yield, R_f = 0.85 in 9:1 hexanes:EtOAc) as a colorless oil: ¹H NMR (400 MHz, CDCl₃) δ 7.35-7.31 (m, 2H), 7.26-7.22 (m, 3H), 6.49 (dd, 1H, J = 14.0, 6.4 Hz), 4.60 (q, 1H, J = 6.8 Hz), 4.47 (dd, 1H, J = 14.0, 1.6 Hz), 4.17 (dd, 1H, J = 6.8, 1.6 Hz), 2.76 (t, 2H, J = 7.6 Hz), 2.27 (td, 2H, J = 7.2, 1.6 Hz), 1.87 (quintet, 2H, J = 7.2 Hz), 1.54 (d, 3H, J = 6.8 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 150.0, 141.8, 128.8, 128.7, 126.2, 89.8, 86.2, 80.3, 65.3, 35.0, 30.5, 22.5, 18.4; IR (film) 2936, 1636, 1616, 1331, 1190, 1079 cm⁻¹; HRMS (EI⁺) calc'd for [C₁₅H₁₈O]⁺: m/z 214.1358, found 214.1354; Anal calc'd for C₁₅H₁₈O: C, 84.07; H, 8.47; found: C, 84.37; H, 8.43.

5a (Table 1, entry 1)

The crude mixture was purified by flash column chromatography (1% TEA in 20:1 hexanes:EtOAc eluent) to afford the desired vinyl ether (0.644 g, 56% yield, R_f = 0.47 in 3:1 hexanes:EtOAc) as a colorless oil: ^1H NMR (400 MHz, CDCl_3) δ 7.77 (d, 2H, J = 8.4 Hz), 7.33-7.25 (m, 4H), 7.21-7.15 (m, 3H), 6.39 (dd, 1H, J = 14.0, 7.2 Hz), 4.36 (dd, 1H, J = 12.4, 1.6 Hz), 4.35-4.31 (m, 1H), 4.09 (dd, 1H, J = 6.4, 1.6 Hz), 4.03 (t, 2H, J = 6.4 Hz), 2.76 (t, 2H, J = 7.2 Hz), 2.43 (s, 3H), 2.21 (td, 2H, J = 7.2, 2.0 Hz), 2.13-1.95 (m, 2H), 1.79-1.72 (m, 2H), 1.58-1.51 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 149.8, 144.8, 141.1, 133.1, 129.9, 128.5, 128.5, 127.9, 126.1, 89.6, 86.3, 78.8, 69.9, 68.1, 37.2, 31.3, 27.9, 24.4, 21.7, 18.1; IR (film) 2953, 1359, 1176 cm^{-1} ; Anal calc'd for $\text{C}_{24}\text{H}_{28}\text{O}_4\text{S}$: C, 69.87; H, 6.84; S, 7.77; found: C, 70.0; H, 6.83; S, 8.11.

5b (Table 1, entry 2)

The crude mixture was purified by flash column chromatography (9:1 hexanes:EtOAc eluent) to afford the desired vinyl ether (0.280 g, 87% yield, R_f = 0.50 in 3:1 hexanes:EtOAc) as a colorless oil: ^1H NMR (400 MHz, CDCl_3) δ 7.33-7.27 (m, 2H), 7.21-7.18 (m, 3H), 6.41 (dd, 1H, J = 14.0, 6.8 Hz), 4.38 (dd, 1H, J = 14.0, 1.6 Hz), 4.39-4.35 (m, 1H), 4.12 (dd, 1H, J = 6.4, 1.6 Hz), 2.78 (t, 2H, J = 7.2 Hz), 2.37 (t, 2H, J = 6.8 Hz), 2.30 (td, 2H, J = 6.8, 2.0 Hz), 2.16-1.98 (m, 2H), 1.82-1.75 (m, 2H), 1.71-1.63 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 149.8, 141.1, 128.6, 128.5, 126.1, 119.4, 89.6, 85.8, 79.1, 68.1, 37.2, 31.3, 27.3, 24.4, 18.0, 16.8; IR (film) 2919, 2244, 1636, 1164 cm^{-1} ; HRMS (EI^+) calc'd for $[\text{C}_{18}\text{H}_{21}\text{NO}]^+$: m/z 267.1623, found 267.1620; Anal calc'd for $\text{C}_{18}\text{H}_{21}\text{NO}$: C, 80.86; H, 7.92; N, 5.24; found: C, 80.55; H, 8.08; N, 5.19.

5c (Table 1, entry 3)

The crude mixture was purified by flash column chromatography (1% TEA in 50:1 hexanes:EtOAc eluent) to afford the desired vinyl ether (0.675 g, 60% yield, R_f = 0.86 in 3:1 hexanes:EtOAc) as a colorless oil: ^1H NMR (400 MHz, CDCl_3) δ 7.31-7.27 (m, 2H), 7.21-7.18 (m, 3H), 6.43 (dd, 1H, J = 14.0, 6.8 Hz), 4.39 (dd, 1H, J = 14.0, 1.6 Hz), 4.35 (td, 1H, J = 6.8, 1.6 Hz), 4.11 (dd, 1H, J = 6.8, 1.6 Hz), 2.78 (t, 2H, J = 7.2 Hz), 2.15-1.98 (m, 2H), 1.31-1.24 (m, 1H), 0.82-0.78 (m, 2H), 0.71-0.68 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 149.8, 141.2, 128.6, 128.5, 126.0, 90.7, 89.5, 73.1, 68.4, 37.3, 31.3, 8.5, 8.4, -0.5; IR (film) 3025, 2241, 1634, 1616, 1187, 1164, 1052 cm^{-1} ; Anal calc'd for $\text{C}_{16}\text{H}_{18}\text{O}$: C, 84.91; H, 8.02; found: C, 85.05; H, 8.18.

5d (Table 1, entry 4)

The crude mixture was purified by flash column chromatography (2% TEA in hexanes eluent) to afford the desired vinyl ether (0.629 g, 85% yield, R_f = 0.86 in 3:1 hexanes:EtOAc) as a colorless oil: ^1H NMR (400 MHz, CDCl_3) δ 7.38-7.27 (m, 2H), 7.21-7.16 (m, 3H), 6.44 (dd, 1H, J = 14.0, 6.4 Hz), 4.42-4.37 (m, 2H), 4.10 (dd, 1H, J = 6.8, 2.0 Hz), 2.79 (t, 2H, J = 7.2 Hz), 2.46-2.40 (m, 1H), 2.17-1.98 (m, 2H), 1.80-1.76 (m, 2H), 1.73-1.66 (m, 2H), 1.52-1.41 (m, 3H), 1.38-1.22 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 149.8, 141.3, 128.6, 128.5, 126.0, 91.8, 89.5, 77.8, 68.4, 37.4, 32.6, 31.4, 29.0, 25.9, 24.7; IR (film) 2929, 2854, 2232, 1635, 1615, 1449, 1188, 1165 cm^{-1} ; HRMS (FAB^+) calc'd for $[\text{C}_{19}\text{H}_{24}\text{O} + \text{Li}]^+$: m/z 275.1987, found 275.1988; Anal calc'd for $\text{C}_{19}\text{H}_{24}\text{O}$: C, 85.03; H, 9.01; found: C, 85.18; H, 9.13.

5e (Table 1, entry 5)

The crude mixture was purified by flash column chromatography (1% TEA in hexanes eluent) to afford the desired vinyl ether (0.759 g, 68% yield, R_f = 0.91 in 3:1 hexanes:EtOAc) as a colorless oil: ^1H NMR (400 MHz, CDCl_3) δ ; ^{13}C NMR (100 MHz, CDCl_3) δ ; IR (film) 2968, 2238, 1636, 1616, 1189, 1165 cm^{-1} ; Anal calc'd for $\text{C}_{17}\text{H}_{22}\text{O}$: C, 84.25; H, 9.15; found: C, 84.50; H, 9.49.

5f (Table 1, entry 6)

The crude mixture was purified by flash column chromatography (2% TEA in hexanes eluent) to afford the desired vinyl ether (0.746 g, 67% yield, R_f = 0.67 in 9:1 hexanes:EtOAc) as a colorless oil: ^1H NMR (400 MHz, CDCl_3) δ 7.31-7.26 (m, 2H), 7.21-7.16 (m, 3H), 6.47 (dd, 1H, J = 14.4, 6.8 Hz), 4.42 (dd, 1H, J = 14.0, 1.6 Hz), 4.22 (dt, 1H, J = 5.6, 2.0 Hz), 4.10 (dd, 1H, J = 6.8, 1.6 Hz), 2.73 (t, 2H, J = 7.6 Hz), 2.25 (td, 2H, J = 6.8, 2.0 Hz), 2.00 (septet, 1H, J = 6.0 Hz), 1.84 (quintet, 2H, J = 7.2 Hz), 1.05 (d, 3H, J = 6.8 Hz), 1.02 (d, 3H, J = 6.8 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 150.3, 141.6, 128.6, 128.4, 125.9, 89.1, 87.3, 77.4, 74.7, 34.8, 33.1, 30.4, 18.4, 18.2, 17.7; IR (film) 2940, 1636, 1616, 1495, 1453, 1173, 1027 cm^{-1} ; HRMS (EI^+) calc'd for $[\text{C}_{17}\text{H}_{22}\text{O}]^+$: m/z 242.1671, found 242.1670; Anal calc'd for $\text{C}_{17}\text{H}_{22}\text{O}$: C, 84.25; H, 9.15; found: C, 84.68; H, 9.36.

5i (Table 1, entry 9)

The crude mixture was purified by flash column chromatography (1% TEA in hexanes eluent) to afford the desired vinyl ether (0.863 g, 76% yield, R_f = 0.87 in 3:1 hexanes:EtOAc) as a colorless oil: ^1H NMR (400 MHz, CDCl_3) δ 6.42 (dd, 1H, J = 14.0, 6.8 Hz), 5.09 (tt, 1H, J = 7.2, 1.6 Hz), 4.40-4.34 (m, 2H), 4.08 (dd, 1H, J = 6.8, 1.6 Hz), 2.22 (td, 2H, J = 7.2, 2.0 Hz), 2.13 (q, 2H, J = 7.6 Hz), 1.85-1.70 (m, 2H), 1.68 (s, 3H), 1.60 (s, 3H), 1.52-1.47 (m, 2H), 1.46-1.35 (m, 2H), 0.89 (t, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 149.9, 132.7, 123.1, 89.3, 87.2, 78.2, 68.7, 35.8, 30.7, 25.8, 23.7, 21.9, 18.4, 17.7, 13.6; IR (film) 2959, 2930, 1635, 1614, 1189 cm^{-1} ; Anal calc'd for $\text{C}_{15}\text{H}_{24}\text{O}$: C, 81.76; H, 10.98; found: C, 81.95; H, 11.36.

7a

The crude mixture was purified by flash column chromatography (1% TEA in 50:1 hexanes:EtOAc eluent) to afford the desired vinyl ether (0.396 g, 93% yield, R_f = 0.88 in 3:1 hexanes:EtOAc) as a colorless oil: ^1H NMR (400 MHz, CDCl_3) δ 7.30-7.26 (m, 2H), 7.20-7.18 (m, 3H), 6.44 (d, 1H, J = 12.4 Hz), 5.13 (dt, 1H, J = 12.4, 6.8 Hz), 4.34 (tt, 1H, J = 6.4, 1.6 Hz), 4.11 (dd, 2H, J = 6.8, 1.2 Hz), 2.78 (t, 2H, J = 6.8 Hz), 2.22 (td, 2H, J = 6.8, 2.0 Hz), 2.14-1.97 (m, 2H), 1.53-1.45 (m, 2H), 1.45-1.37 (m, 2H), 0.91 (t, 3H, J = 7.2 Hz), 0.90 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 146.4, 141.3, 128.5, 128.4, 126.0, 106.1, 87.7, 77.9, 69.2, 61.1, 37.4, 31.3, 30.7, 26.0, 21.9, 18.4 (2), 13.6, -4.9; IR (film) 2955, 2930, 2858, 1672, 1655, 1463, 1169, 1058 cm^{-1} ; Anal calc'd for $\text{C}_{24}\text{H}_{38}\text{O}_2\text{Si}$: C, 74.55; H, 9.91; found: C, 74.66; H, 10.21.

7b

The crude mixture was purified by flash column chromatography (1% TEA in 15:1 hexanes:EtOAc eluent) to afford the desired vinyl ether (0.314 g, 91% yield, R_f = 0.62 in 3:1 hexanes:EtOAc) as a colorless oil: ^1H NMR (400 MHz, CDCl_3) δ 7.30-7.26 (m, 2H), 7.21-7.17 (m, 3H), 6.58 (d, 1H, J = 12.4 Hz), 5.14 (dt, 1H, J = 12.4, 8.0 Hz), 4.53-4.45 (m, 2H), 4.37 (tt, 1H, J = 6.4, 1.6 Hz), 2.77 (t, 2H, J = 7.2 Hz), 2.23 (td, 2H, J = 6.8, 2.0 Hz), 2.14-1.98 (m, 2H), 2.03 (s, 3H), 1.54-1.46 (m, 2H), 1.46-1.37 (m, 2H), 0.91 (t, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 171.0, 150.2, 141.1, 128.5, 128.5, 126.1, 100.6, 88.3, 77.4, 69.6, 62.6, 37.3, 31.3, 30.6, 21.9, 21.2, 18.4, 13.6; IR (film) 2955, 2933, 2871, 2235, 1739, 1671, 1658, 1454, 1381, 1363, 1231, 1177 cm^{-1} ; HRMS (FAB^+) calc'd for $[\text{C}_{20}\text{H}_{26}\text{O}_3 + \text{Li}]^+$: m/z 321.2042, found 321.2041; Anal calc'd for $\text{C}_{20}\text{H}_{26}\text{O}_3$: C, 76.40; H, 8.33; found: C, 76.33; H, 8.52.

9a

The crude mixture was purified by flash column chromatography (1% TEA in 3:1 hexanes:EtOAc eluent) to afford the desired vinyl ether (0.217 g, 50% yield, R_f = 0.12 in 3:1 hexanes:EtOAc) as a colorless oil: ^1H

NMR (400 MHz, C_6D_6) δ 5.02 (t, 1H, J = 8.0 Hz), 4.69 (d, 2H, J = 8.0 Hz), 4.42-4.36 (m, 1H), 3.44 (t, 2H, J = 6.0 Hz), 2.31 (t, 1H, J = 7.2 Hz), 2.30 (t, 1H, J = 7.2 Hz), 1.73-1.65 (m, 2H), 1.70 (s, 3H), 1.40 (d, 3H, J = 2.0 Hz), 1.35 (d, 3H, J = 6.4 Hz); ^{13}C NMR (100 MHz, C_6D_6) δ 170.1, 160.1, 94.7, 81.3, 78.6, 62.5, 61.1, 61.0, 30.5, 26.5, 22.1, 20.4, 2.8; IR (film) 3422, 2936, 2247, 1736, 1657, 1371, 1239, 1073 cm^{-1} .

9b

The crude mixture was purified by flash column chromatography (2% TEA in 3:1 hexanes:EtOAc eluent) to afford the desired vinyl ether (0.158 g, 30% yield, R_f = 0.13 in 3:1 hexanes:EtOAc) as a colorless oil: 1H NMR (500 MHz, C_6D_6) δ 5.03 (t, 1H, J = 8.5 Hz), 4.68 (d, 2H, J = 8.0 Hz), 4.44-4.40 (m, 1H), 3.36 (t, 2H, J = 6.5 Hz), 2.21 (t, 2H, J = 7.5 Hz), 1.72 (s, 3H), 1.58 (quintet, 2H, J = 8.0 Hz), 1.44-1.35 (m, 2H), 1.40 (d, 3H, J = 2.0 Hz), 1.37 (d, 3H, J = 6.5 Hz); ^{13}C NMR (125 MHz, C_6D_6) δ 170.1, 160.6, 94.2, 81.5, 78.6, 62.4, 61.9, 61.0, 32.0, 29.9, 23.9, 22.1, 20.4, 2.8; IR (film) 3416, 2936, 2247, 1735, 1657, 1371, 1237 cm^{-1} ; HRMS (EI $^+$) calc'd for $[C_{12}H_{19}O_3]^+$: m/z 211.1334, found 211.1333.

Characterization Data for Pyran Hemiacetals 4, 6a-j, 8a-b:

4

The crude mixture was purified by flash column chromatography (5:1 hexanes:EtOAc eluent) to afford the desired pyran (0.181 g, 84% yield, 1.2:1.0 dr, R_f = 0.10 in 5:1 hexanes:EtOAc) as a colorless oil: 1H NMR (400 MHz, $CDCl_3$) The following were observed for the mixture of diastereomers δ 7.30-7.25 (m, 4H), 7.20-7.15 (m, 6H), 5.39 (s, 2H), 5.28 (s, 1H), 4.99 (q, 1H, J = 6.0 Hz), 4.51-4.50 (br s, 1H), 4.38-4.36 (br s, 1H), 3.45 (m, 1H), 3.00 (m, 1H), 2.68-2.58 (m, 4H), 2.36 (d, 1H, J = 17.2 Hz), 2.15-2.14 (m, 2H), 2.08-2.04 (m, 3H), 1.97 (d, 1H, J = 17.2 Hz), 1.81-1.73 (m, 4H), 1.29 (d, 3H, J = 6.4 Hz), 1.26 (d, 3H, J = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) The following were observed for the major diastereomer δ 93.6, 70.5; The following were observed for the minor diastereomer δ 90.4, 64.2; The following were observed for the mixture of diastereomers δ 142.3, 142.2, 134.0, 131.7, 128.4 (2), 128.3 (2), 125.8 (2), 124.3, 123.5, 36.3, 35.9, 35.6, 35.3 (2), 33.5, 28.7 (2), 21.4, 21.1; IR (film) 3330, 2929, 1452, 1371, 1158, 1096 cm^{-1} ; HRMS (EI $^+$) calc'd for $[C_{15}H_{20}O_2]^+$: m/z 232.1463, found 232.1458; Anal calc'd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68; found: C, 75.46; H, 8.61.

6a (Table 1, entry 1)

The crude mixture was purified by flash column chromatography (2:1 hexanes:EtOAc eluent) to afford the desired pyran (92 mg, 89% yield, 1.2:1.0 dr, R_f = 0.13 in 3:1 hexanes:EtOAc) as a pale yellow oil: 1H NMR (400 MHz, $CDCl_3$) The following were observed for the mixture of diastereomers δ 7.77 (d, 4H, J = 8.4 Hz), 7.31 (d, 4H, J = 8.4 Hz), 7.28-7.24 (m, 4H), 7.19-7.14 (m, 6H), 5.39 (d, 1H, J = 2.4 Hz), 5.34 (s, 1H), 5.24 (s, 1H), 4.95 (t, 1H, J = 5.6 Hz), 4.33 (s, 1H), 4.21 (s, 1H), 4.01 (t, 2H, J = 6.4 Hz), 4.01 (t, 2H, J = 6.0 Hz), 3.59 (s, 1H), 3.11 (s, 1H), 2.80-2.63 (m, 4H), 2.42 (s, 6H), 2.29 (d, 1H, J = 17.6 Hz), 2.05 (s, 2H), 1.93-1.79 (m, 9H), 1.66-1.57 (m, 4H), 1.46-1.39 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) The following were observed for the major diastereomer δ 93.6, 73.5; The following were observed for the minor diastereomer δ 90.4, 67.5; The following were observed for the mixture of diastereomers δ 144.8, 144.8, 142.2, 142.1, 134.2 (2), 133.1, 132.0, 129.9 (2), 128.5, 128.5, 128.4 (2), 127.9 (2), 125.8 (2), 123.4, 122.6, 70.4, 70.4, 37.2, 36.9, 36.1, 35.8, 35.7, 33.6, 31.4, 31.3, 28.3 (2), 22.9, 22.8, 21.7 (2); Anal calc'd for $C_{24}H_{30}O_5S$: C, 66.95; H, 7.02; S, 7.45; found: C, 64.43; H, 7.18.

6b (Table 1, entry 2)

The crude mixture was purified by flash column chromatography (2:1 hexanes:EtOAc eluent) to afford the desired pyran (94 mg, 88% yield, 1.1:1.0 dr, R_f = 0.07 in 3:1 hexanes:EtOAc) as a colorless oil: ^1H NMR (400 MHz, CDCl_3) The following were observed for the mixture of diastereomers δ 7.37-7.30 (m, 4H), 7.26-7.20 (m, 6H), 5.46 (s, 2H), 5.35 (s, 1H), 5.02 (s, 1H), 4.42 (s, 1H), 4.29 (s, 1H), 4.08-3.90 (br s, 1H), 3.58-3.42 (br s, 1H), 2.87-2.70 (m, 4H), 2.41-2.34 (m, 5H), 2.17 (s, 2H), 2.10-1.87 (m, 9H), 1.71-1.57 (m, 8H); ^{13}C NMR (100 MHz, CDCl_3) The following were observed for the major diastereomer δ 93.5, 73.5; The following were observed for the minor diastereomer δ 90.3, 67.5; The following were observed for the mixture of diastereomers δ 142.2, 142.1, 134.0, 131.8, 128.5, 128.5, 128.4 (2), 125.8 (2), 123.6, 122.8, 119.7, 119.7, 37.2, 36.9, 36.0, 35.7, 35.6, 33.6, 31.4, 31.3, 26.0, 25.9, 24.8 (2), 17.0 (2); IR (film) 3410, 2929, 2246, 1453, 1120 cm^{-1} ; Anal calc'd for $\text{C}_{18}\text{H}_{23}\text{NO}_2$: C, 75.76; H, 8.12; N, 4.91; found: C, 73.85; H, 8.21; N, 4.90.

6c (Table 1, entry 3)

The crude mixture was purified by flash column chromatography (6:1 hexanes:EtOAc eluent) to afford the desired pyran (99 mg, 92% yield, 1.2:1.0 dr, R_f = 0.31 in 3:1 hexanes:EtOAc) as a colorless oil: ^1H NMR (400 MHz, CDCl_3) The following were observed for the mixture of diastereomers δ 7.29-7.25 (m, 4H), 7.21-7.16 (m, 6H), 5.42 (s, 2H), 5.32 (s, 1H), 4.96 (q, 1H, J = 6.0 Hz), 4.37 (s, 1H), 4.25 (s, 1H), 3.94 (d, 1H, J = 6.0 Hz), 3.40 (d, 1H, J = 4.8 Hz), 2.83-2.65 (m, 4H), 2.58 (d, 1H, J = 17.6 Hz), 2.05-2.04 (m, 2H), 1.98-1.81 (m, 5H), 1.38-1.32 (m, 2H), 0.66-1.56 (m, 4H), 0.51-0.43 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) The following were observed for the major diastereomer δ 93.7, 73.7; The following were observed for the minor diastereomer δ 90.4, 67.8; The following were observed for the mixture of diastereomers δ 142.3, 142.1, 136.1, 133.8, 128.5, 128.5, 128.4 (2), 125.8 (2), 121.3, 120.5, 37.3, 37.0, 33.9, 32.0, 31.4, 31.3, 16.8, 16.4, 4.8, 4.7, 4.2 (2); IR (film) 3393, 2926, 1666, 1603, 1453, 1070 cm^{-1} ; HRMS (EI^+) calc'd for $[\text{C}_{16}\text{H}_{20}\text{O}_2]^+$: m/z 244.1463, found 244.1462.

6d (Table 1, entry 4)

The crude mixture was purified by flash column chromatography (9:1 hexanes:EtOAc eluent) to afford the desired pyran (85 mg, 80% yield, 1.3:1.0 dr, R_f = 0.42 in 3:1 hexanes:EtOAc) as a colorless oil: ^1H NMR (400 MHz, CDCl_3) The following were observed for the mixture of diastereomers δ 7.31-7.27 (m, 4H), 7.23-7.17 (m, 6H), 5.43 (s, 1H), 5.39 (s, 1H), 5.28 (s, 1H), 5.00-4.96 (m, 1H), 4.40 (br s, 1H), 4.28 (br s, 1H), 3.84 (d, 1H, J = 6.0 Hz), 3.30 (d, 1H, J = 5.2 Hz), 2.84-2.67 (m, 4H), 2.40 (d, 1H, J = 17.2 Hz), 2.23-2.12 (m, 2H), 2.03 (br d, 1H, J = 17.2 Hz), 1.94-1.68 (m, 16H), 1.34-1.08 (m, 10H); ^{13}C NMR (100 MHz, CDCl_3) The following were observed for the major diastereomer δ 93.8, 73.7; The following were observed for the minor diastereomer δ 90.6, 67.8; The following were observed for the mixture of diastereomers δ 142.2, 142.1, 140.2, 137.8, 128.5, 128.5, 128.3 (2), 125.7 (2), 120.8, 120.0, 44.5, 44.3, 37.3, 37.0, 34.4, 32.4, 31.6, 31.5, 31.3, 31.2, 31.1, 31.1, 26.5 (2), 26.4, 26.4, 26.3, 26.3; IR (film) 3400, 2924, 2851, 1450, 1065 cm^{-1} ; Anal calc'd for $\text{C}_{19}\text{H}_{26}\text{O}_2$: C, 79.68; H, 9.15; found: C, 78.43; H, 9.21.

6e (Table 1, entry 5)

The crude mixture was purified by flash column chromatography (9:1 hexanes:EtOAc eluent) to afford the desired pyran (64 mg, 60% yield, 1.2:1.0 dr, R_f = 0.44 in 3:1 hexanes:EtOAc) as a colorless oil: ^1H NMR (400 MHz, CDCl_3) The following were observed for the mixture of diastereomers δ 7.31-7.27 (m, 4H), 7.24-7.17 (m, 6H), 5.46 (s, 2H), 5.32 (s, 1H), 4.97 (ddd, 1H, J = 8.8, 6.0, 3.2 Hz), 4.41 (m, 1H), 4.30 (br s, 1H), 3.83 (d, 1H, J = 6.0 Hz), 3.27 (d, 1H, J = 5.2 Hz), 2.86-2.68 (m, 4H), 2.42-2.31 (m, 2H), 2.16-2.08 (m, 2H), 1.94-1.87 (m, 4H), 1.06 (s, 9H), 1.04 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) The following were observed for the major diastereomer δ 94.0, 73.8; The following were observed for the minor diastereomer δ 90.7, 68.2; The following were observed for the mixture of diastereomers δ 143.0, 142.2, 142.2, 140.6,

128.5, 128.5, 128.3 (2), 125.7 (2), 119.5, 118.9, 37.4, 37.0, 34.8, 34.7, 32.1, 31.4, 31.3, 30.2, 28.5, 28.4; IR (film) 3393, 2961, 1454, 1362, 1076 cm^{-1} ; Anal calc'd for $\text{C}_{17}\text{H}_{24}\text{O}_2$: C, 78.42; H, 9.29; found: C, 78.06; H, 9.59.

6f (Table 1, entry 6)

The crude mixture was purified by flash column chromatography (6:1 hexanes:EtOAc eluent) to afford the desired pyran (96 mg, 90% yield, 1.1:1.0 dr, R_f = 0.44 in 3:1 hexanes:EtOAc) as a colorless oil: ^1H NMR (300 MHz, CDCl_3) The following were observed for the mixture of diastereomers δ 7.32-7.25 (m, 4H), 7.21-7.17 (m, 6H), 5.44 (s, 2H), 5.33 (d, 1H, J = 1.2 Hz), 4.96 (q, 1H, J = 5.7 Hz), 4.16 (br s, 1H), 4.07 (t, 1H, J = 1.5 Hz), 3.88 (d, 1H, J = 6.0 Hz), 3.36 (d, 1H, J = 4.2 Hz), 2.64-2.53 (m, 4H), 2.36 (br d, 1H, J = 17.1 Hz), 2.12-1.70 (m, 13H), 0.97-0.93 (m, 12H); ^{13}C NMR (100 MHz, CDCl_3) The following were observed for the major diastereomer δ 93.9, 79.5; The following were observed for the minor diastereomer δ 90.9, 72.8; The following were observed for the mixture of diastereomers δ 142.6, 142.6, 135.6, 133.0, 128.7 (2), 128.6 (2), 126.1 (2), 121.6, 120.7, 37.1, 36.6, 36.2, 35.7, 35.6, 34.0, 32.9, 32.8, 29.2, 29.2, 18.3, 18.3, 18.0, 18.0; IR (film) 3389, 2928, 1603, 1453, 1029 cm^{-1} ; Anal calc'd for $\text{C}_{17}\text{H}_{24}\text{O}_2$: C, 78.42; H, 9.29; found: C, 76.85; H, 9.25.

6g (Table 1, entry 7)

The crude mixture was purified by flash column chromatography (9:1 hexanes:EtOAc eluent) to afford the desired pyran (103 mg, 95% yield, 1.3:1.0 dr, R_f = 0.50 in 3:1 hexanes:EtOAc) as a colorless oil: ^1H NMR (400 MHz, CDCl_3) The following were observed for the mixture of diastereomers δ 7.36-7.25 (m, 10H), 5.44 (s, 1H), 5.37-5.34 (m, 2H), 4.89 (t, 1H, J = 5.6 Hz), 4.61 (s, 1H), 4.48-4.45 (m, 1H), 4.00 (br s, 1H), 3.56 (br s, 1H), 3.00 (dd, 1H, J = 13.6, 6.8 Hz), 2.93 (dd, 1H, J = 13.6, 7.6 Hz), 2.87-2.80 (m, 2H), 2.34 (d, 1H, J = 18.0 Hz), 2.12 (t, 2H, J = 2.8 Hz), 2.05-1.94 (m, 5H), 1.47-1.27 (m, 8H), 0.95 (t, 3H, J = 7.2 Hz), 0.95 (t, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, CDCl_3) The following were observed for the major diastereomer δ 93.6, 75.4; The following were observed for the minor diastereomer δ 90.5, 69.4; The following were observed for the mixture of diastereomers δ 138.4, 138.1, 135.4, 133.3, 129.6, 129.6, 128.3, 128.3, 126.3, 126.3, 121.8, 121.1, 42.3, 41.9, 36.7, 36.3, 35.5, 33.6, 29.3, 29.2, 22.3, 22.2, 14.0 (2); IR (film) 3398, 2926, 1453, 1126, 1053 cm^{-1} ; HRMS (EI^+) calc'd for $[\text{C}_{16}\text{H}_{22}\text{O}_2\text{-H}_2\text{O}]^+$: m/z 228.1514, found 228.1514.

6h (Table 1, entry 8)

The crude mixture was purified by flash column chromatography (15:1 hexanes:EtOAc eluent) to afford the desired pyran (82 mg, 77% yield, 1.1:1.0 dr, R_f = 0.49 in 3:1 hexanes:EtOAc) as a colorless oil: ^1H NMR (300 MHz, CDCl_3) The following were observed for the mixture of diastereomers δ 5.40-5.39 (m, 2H), 5.34 (d, 1H, J = 1.2 Hz), 5.07 (q, 1H, J = 3.6 Hz), 4.36-4.25 (m, 3H), 3.69-3.55 (m, 5H), 2.31 (d, 1H, J = 16.2 Hz), 2.20-1.92 (m, 7H), 1.42-1.23 (m, 8H), 0.87 (s, 18H), 0.87 (t, 6H, J = 6.3 Hz), 0.06 (s, 3H), 0.05 (s, 3H), 0.04 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) The following were observed for the major diastereomer δ 92.3, 74.7; The following were observed for the minor diastereomer δ 90.8, 70.1; The following were observed for the mixture of diastereomers δ 135.9, 134.3, 119.3, 119.0, 66.4 (2), 37.0, 36.8, 35.6, 34.1, 29.4, 29.4, 26.2, 26.1, 22.5, 22.5, 18.7, 18.6, 14.2 (2), -5.2, -5.1, -5.0, -5.0; IR (film) 3407, 2928, 1463, 1254, 1139, 1084 cm^{-1} ; Anal calc'd for $\text{C}_{16}\text{H}_{32}\text{O}_3\text{Si}$: C, 63.95; H, 10.73; found: C, 63.81; H, 10.92.

6i (Table 1, entry 9)

The crude mixture was purified by flash column chromatography (12:1 hexanes:EtOAc eluent) to afford the desired pyran (99 mg, 92% yield, 1.2:1.0 dr, R_f = 0.60 in 3:1 hexanes:EtOAc) as a colorless oil: ^1H NMR (400 MHz, CDCl_3) The following were observed for the mixture of diastereomers δ 5.35 (s, 2H),

5.24 (d, 1H, $J = 1.2$ Hz), 5.11-5.04 (m, 2H), 4.92 (t, 1H, $J = 6.0$ Hz), 4.30 (s, 1H), 4.20-4.03 (br s, 1H), 4.18 (t, 1H, $J = 1.2$ Hz), 3.70-3.50 (br s, 1H), 2.30 (d, 1H, $J = 17.2$ Hz), 2.10-1.90 (m, 11H), 1.65 (s, 6H), 1.57 (s, 6H), 1.57-1.47 (m, 4H), 1.40-1.21 (m, 8H), 0.86 (t, 6H, $J = 7.2$ Hz); ^{13}C NMR (100 MHz, CDCl_3) The following were observed for the major diastereomer δ 93.7, 74.0; The following were observed for the minor diastereomer δ 90.4, 67.9; The following were observed for the mixture of diastereomers δ 135.0, 132.6, 131.8, 131.8, 124.1, 124.1, 122.7, 121.9, 36.7, 36.3, 35.9, 35.6, 35.3, 33.8, 29.3, 29.2, 25.7 (2), 23.7, 23.6, 22.3, 22.2, 17.7 (2), 13.9 (2); IR (film) 3398, 2926, 1671, 1451, 1377, 1125, 1073 cm^{-1} ; Anal calc'd for $\text{C}_{15}\text{H}_{26}\text{O}_2$: C, 75.58; H, 10.99; found: C, 75.81; H, 11.18.

6j (Table 1, entry 10)

The crude mixture was purified by flash column chromatography (4:1 hexanes:EtOAc eluent) to afford the desired pyran (37 mg, 83% yield, 1.0:1.0 dr, $R_f = 0.22$ in 3:1 hexanes:EtOAc) as a yellow/brown solid: ^1H NMR (400 MHz, CDCl_3) The following were observed for the mixture of diastereomers δ 7.98 (d, 2H, $J = 8.4$ Hz), 7.75 (d, 2H, $J = 8.4$ Hz), 7.75 (d, 2H, $J = 8.4$ Hz), 7.51 (dt, 2H, $J = 8.0, 1.2$ Hz), 7.47 (s, 1H), 7.44 (s, 1H), 7.30 (t, 2H, $J = 7.2$ Hz), 7.24-7.18 (m, 6H), 5.40 (d, 1H, $J = 2.8$ Hz), 5.37 (s, 1H), 5.27 (s, 1H), 4.96 (dd, 1H, $J = 7.6, 3.6$ Hz), 4.63 (s, 1H), 4.51 (m, 1H), 3.01-2.83 (m, 5H), 2.32 (s, 6H), 2.32-2.23 (m, 2H), 2.09-2.02 (m, 2H), 1.96-1.92 (m, 5H), 1.44-1.17 (m, 8H), 0.86 (t, 6H, $J = 7.2$ Hz); ^{13}C NMR (100 MHz, CDCl_3) The following were observed for the mixture of diastereomers δ 135.7, 135.3, 135.0, 135.1, 133.5 (2), 131.3 (2), 131.2 (2), 129.8, 129.7, 126.7, 126.7, 124.5, 124.5, 124.3, 124.2, 123.0 (2), 121.7, 121.0, 119.7 (2), 119.1, 118.9, 113.6 (2), 93.5, 90.6, 73.4, 67.4, 36.6, 36.2, 35.6, 33.5, 31.3, 30.9, 29.1, 29.1, 22.1, 22.1, 21.5 (2), 19.3 (2); IR (film) 3424, 2927, 1446, 1368, 1172, 1121 cm^{-1} ; Anal calc'd for $\text{C}_{25}\text{H}_{29}\text{NO}_4\text{S}$: C, 68.31; H, 6.65; N, 3.19; S, 7.29; found: C, 67.92; H, 6.84; N, 3.09.

8a

The crude mixture was purified by flash column chromatography (21:1 to 15:1 hexanes:EtOAc eluent) to afford the desired pyran (44 mg, 85% yield, 4.0:1.0 anomeric mixture, $R_f = 0.66$ in 3:1 hexanes:EtOAc) as a colorless oil: ^1H NMR (400 MHz, C_6D_6) The following were observed for the major diastereomer δ 5.58 (s, 1H), 5.26 (s, 1H), 0.97 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); The following were observed for the minor diastereomer δ 5.89 (d, 1H, $J = 9.2$ Hz), 5.10-5.06 (m, 2H), 0.89 (s, 9H), 0.00 (s, 3H), 0.00 (s, 3H); The following were observed for the mixture of diastereomers δ 7.20-7.04 (m, 10H), 4.33-4.15 (m, 3H), 3.76-3.66 (m, 2H), 2.88-2.73 (m, 4H), 2.46-2.36 (m, 3H), 1.93-1.79 (m, 9H), 1.38-1.16 (m, 8H), 0.87-0.77 (m, 6H); ^{13}C NMR (100 MHz, C_6D_6) The following were observed for the major diastereomer δ 142.4, 133.2, 128.5, 128.3, 125.7, 124.0, 91.4, 67.1, 64.2, 46.2, 37.6, 35.0, 31.6, 29.6, 25.8, 22.3, 18.2, 13.8, -5.5, -5.6; The following were observed for the minor diastereomer δ 142.3, 135.3, 128.6, 128.3, 126.0, 125.7, 96.7, 73.8, 63.5, 44.3, 37.7, 34.5, 31.5, 29.7, 25.5, 22.3, 17.9, 13.8, -5.9, -6.0; IR (film) 3407, 2929, 1455, 1256, 1094 cm^{-1} ; HRMS (FAB $^+$) calc'd for $[\text{C}_{24}\text{H}_{40}\text{O}_3\text{Si} + \text{Li}]^+$: m/z 411.2907, found 411.2915.

8b

The crude mixture was purified by flash column chromatography (5:1 hexanes:EtOAc eluent) to afford the desired pyran (47 mg, 88% yield, 5.9:1.0 dr, $R_f = 0.42$ in 3:1 hexanes:EtOAc) as a colorless oil: ^1H NMR (400 MHz, C_6D_6) The following were observed for the major diastereomer δ 5.41 (d, 1H, $J = 4.4$ Hz), 5.25 (s, 1H), 4.35-4.26 (m, 2H), 4.00 (t, 1H, $J = 10$ Hz), 2.38 (d, 1H, $J = 9.6$ Hz), 1.64 (s, 3H); The following were observed for the minor diastereomer δ 5.09 (s, 1H), 4.83 (dd, 1H, $J = 8.0, 2.4$ Hz), 4.47 (dd, 1H, $J = 11.6, 3.6$ Hz), 4.17 (d, 1H, $J = 8.0$ Hz), 4.07-4.02 (m, 1H), 2.26-2.21 (m, 1H), 1.65 (s, 3H); The following were observed for the mixture of diastereomers δ 7.19-7.05 (10H), 2.82-2.70 (m, 6H), 1.91-1.70 (m, 8H), 1.40-1.14 (m, 8H), 0.85 (t, 6H, $J = 7.2$ Hz); ^{13}C NMR (100 MHz, C_6D_6) The following were observed for the major diastereomer δ 169.9, 142.2, 132.2, 128.5, 128.4, 125.8, 124.6, 91.6, 67.0, 64.4, 42.7, 37.3, 34.5, 31.5, 29.5, 22.2, 20.1, 13.8; The following were observed for the minor diastereomer δ 170.6, 142.0, 135.7,

128.5, 128.4, 125.6, 124.6, 94.8, 73.8, 61.4, 42.8, 37.5, 34.1, 31.4, 29.5, 22.3, 20.3, 12.8; IR (film) 3438, 2930, 1740, 1239, 1032 cm^{-1} ; HRMS (FAB⁺) calc'd for $[\text{C}_{20}\text{H}_{28}\text{O}_4 + \text{Li}]^+$: m/z 339.2148, found 339.2155.

Selected nOe cross peaks for major diastereomer **8b** (R = *n*-Bu).

Selected nOe cross peaks for minor diastereomer **8b** (R = *n*-Bu).

Characterization Data for Spiroketal **10a-b**, **12**:

10a

The crude mixture was purified by flash column chromatography (12:1 hexanes:EtOAc eluent) to afford the desired spiroketal (26 mg, 51% yield, >20:1 dr, R_f = 0.52 in 3:1 hexanes:EtOAc) as a colorless oil: ¹H NMR (400 MHz, C_6D_6) δ 5.24 (s, 1H), 4.33-4.27 (m, 1H), 4.20 (d, 2H, J = 5.2 Hz), 3.82-3.77 (m, 1H), 3.71-3.66 (m, 1H), 2.21 (td, 1H, J = 5.6, 2.0 Hz), 2.02-1.93 (m, 2H), 1.74-1.67 (m, 4H), 1.65 (s, 3H), 1.57-1.49 (m, 1H), 1.12 (d, 3H, J = 6.8 Hz); ¹³C NMR (100 MHz, C_6D_6) δ 169.5, 129.8, 126.5, 106.5, 66.8, 66.1, 64.8, 46.2, 35.1, 23.7, 21.7, 21.0, 20.2; HRMS (EI⁺) calc'd for $[\text{C}_{13}\text{H}_{20}\text{O}_4]^+$: m/z 240.1362, found 240.1358; Anal calc'd for $\text{C}_{13}\text{H}_{20}\text{O}_4$: C, 64.98; H, 8.39; found: C, 65.35; H, 8.58.

Selected nOe cross peaks for spiroketal **10a** (R = Me)

10b

The crude mixture was purified by flash column chromatography (12:1 hexanes:EtOAc eluent) to afford the desired spiroketal (36 mg, 71% yield, >20:1 dr, R_f = 0.59 in 3:1 hexanes:EtOAc) as a colorless oil: ¹H NMR (500 MHz, CDCl_3) δ 5.42 (s, 1H), 4.18-4.13 (m, 1H), 4.03 (d, 2H, J = 5.5 Hz), 3.70-3.67 (m, 2H), 2.07-2.05 (m, 1H), 2.03 (s, 3H), 1.92-1.82 (m, 1H), 1.80-1.76 (m, 1H), 1.76 (s, 3H), 1.64-1.60 (m, 1H), 1.58-1.47 (m, 3H), 1.18 (d, 3H, J = 6.5 Hz); ¹³C NMR (125 MHz, CDCl_3) δ 170.9, 128.5, 126.1, 97.0, 65.5, 63.2, 62.4, 47.4, 32.5, 25.1, 22.0, 21.3, 21.1, 18.7; IR (film) 2940, 1742, 1370, 1229, 1087, 1037 cm^{-1} ; HRMS (EI⁺) calc'd for $[\text{C}_{14}\text{H}_{22}\text{O}_4]^+$: m/z 254.1518, found 254.1497; Anal calc'd for $\text{C}_{14}\text{H}_{22}\text{O}_4$: C, 66.12; H, 8.72; found: C, 65.67; H, 8.77.

(±)-12

The crude mixture was purified by flash column chromatography (9:1 hexanes:EtOAc eluent) to afford the desired spiroketal (73 mg, 73% yield, R_f = 0.60 in 3:1 hexanes:EtOAc) as a colorless oil: ¹H NMR (400 MHz, CDCl_3) δ 7.30-7.26 (m, 2H), 7.20-7.16 (m, 3H), 5.43 (s, 1H), 4.29-4.24 (m, 1H), 4.12-4.05 (m, 2H), 3.97-3.87 (m, 2H), 2.72-2.57 (m, 2H), 2.24 (t, 1H, J = 4.8 Hz), 2.18-2.10 (m, 3H), 2.04 (s, 3H), 2.01-2.00 (m, 1H), 1.98-1.83 (m, 3H), 1.80-1.71 (m, 1H), 1.19 (d, 3H, J = 6.8 Hz); ¹³C NMR (100 MHz, CDCl_3) δ

170.8, 142.3, 133.6, 128.4, 128.2, 125.7, 125.6, 106.6, 67.3, 66.3, 65.3, 44.4, 35.5, 35.2, 34.3, 28.9, 23.7, 21.3, 21.0; IR (film) 2930, 1738, 1453, 1368, 1229, 1034 cm^{-1} ; HRMS (FAB⁺) calc'd for $[\text{C}_{21}\text{H}_{28}\text{O}_4 + \text{Li}]^+$: m/z 351.2148, found 351.2147; Anal calc'd for $\text{C}_{21}\text{H}_{28}\text{O}_4$: C, 73.23; H, 8.19; found: C, 73.32; H, 8.59; Racemic assay was determined by chiral HPLC analysis, Chiralcel OD column, 99.5:0.5 hexanes:isopropanol, 1 mL/min; t_R 9.51 min, 12.31 min.

A slower eluting fraction ($R_f = 0.43$ in 3:1 hexanes:EtOAc) was collected and repurified by flash column chromatography (0.5% MeOH in CH_2Cl_2) to afford the diastereomeric spiroketal (9.0 mg, $R_f = 0.16$ in 0.5% MeOH in CH_2Cl_2) as a colorless oil. Resubjecting this material to the optimized reaction conditions led to no change in the ^1H NMR spectrum.

12

The crude mixture was purified by flash column chromatography (9:1 hexanes:EtOAc eluent) to afford the desired spiroketal (58 mg, 58% yield, 10:1 dr, $R_f = 0.57$ in 3:1 hexanes:EtOAc) as a colorless oil: Spectral data were consistent with those described for **12**; Enantiomeric purity was determined by chiral HPLC analysis, Chiralcel OD column, 99.5:0.5 hexanes:isopropanol, 1 mL/min; t_R 9.14 min (minor), 12.04 min (major): 82% ee.

Characterization Data for Pyran Acetal 14:

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The crude mixture was purified by flash column chromatography (40:1 hexanes:EtOAc eluent) to afford the desired pyran (0.107 g, 76% yield, 1.7:1.0 dr, $R_f = 0.56$ in 9:1 hexanes:EtOAc) as a colorless oil: ^1H NMR (400 MHz, CDCl_3) The following were observed for the major diastereomer δ 5.36 (s, 1H), 3.76 (dt, 1H, $J = 10.0, 6.8$ Hz), 2.34 (d, 1H, $J = 17.6$ Hz), 1.92 (d, 1H, $J = 17.2$ Hz), 1.23 (d, 3H, $J = 6.8$ Hz); The following were observed for the minor diastereomer δ 5.29 (s, 1H), 4.61 (dd, 1H, $J = 8.0, 3.2$ Hz), 3.93 (td, 1H, $J = 9.6, 6.8$ Hz), 1.27 (d, 3H, $J = 6.4$ Hz); The following were observed for the mixture of diastereomers δ 7.30-7.25 (m, 4H), 7.20-7.15 (m, 6H), 5.88-5.77 (m, 2H), 5.06-4.94 (m, 5H), 4.32-4.21 (br s, 2H), 3.49-3.43 (m, 2H), 2.61 (t, 4H, $J = 7.6$ Hz), 2.19-2.10 (m, 5H), 2.08-2.00 (m, 5H), 1.81-1.66 (m, 8H); ^{13}C NMR (100 MHz, CDCl_3) The following were observed for the mixture of diastereomers δ 142.4, 142.3, 138.3 (2), 134.0, 132.0, 128.5 (2), 128.3 (2), 125.8, 125.7, 124.6, 123.7, 114.8 (2), 99.3, 96.2, 70.2, 68.2, 66.9, 63.5, 36.3, 36.1, 35.4, 35.3, 34.2, 33.0, 30.5, 30.3, 29.0, 28.9, 28.8, 28.7, 21.6, 21.1; IR (film) 2930, 1369, 1160, 1098, 1040 cm^{-1} ; HRMS (EI⁺) calc'd for $[\text{C}_{20}\text{H}_{28}\text{O}_2]^+$: m/z 300.2089, found 300.2083; Anal calc'd for $\text{C}_{20}\text{H}_{28}\text{O}_2$: C, 79.96; H, 9.39; found: C, 80.11; H, 9.68.

Characterization Data for Allylic Alcohol:

To a solution of propargyl vinyl ether (**R**)-**5f** (100 mg, 0.413 mmol, 94% ee) in 1,4-dioxane (1.4 mL) was added water (7.4 mg, 0.41 mmol) and $[(\text{Ph}_3\text{PAu})_3\text{O}]\text{BF}_4$ (6.1 mg, 4.1 μmol). The resulting mixture was left to stir at rt for 6 h and LiBH_4 (22 mg, 1.0 mmol) was added to afford a deep red solution. Stirring was continued at rt for 15 h and reaction mixture was quenched with H_2O (10 mL). The resulting mixture was extracted with EtOAc (3x, 10 mL) and the combined extracts were washed with brine (1x, 15 mL), dried over Na_2SO_4 , filtered, and concentrated. The crude mixture was purified by flash column chromatography (3:1 hexanes:EtOAc eluent) to afford the desired diol (86 mg, 79% yield, $R_f = 0.09$ in 3:1 hexanes:EtOAc) as a colorless oil: ^1H NMR (400 MHz, C_6D_6) δ 7.19-7.15 (m, 2H), 7.09-7.05 (m, 3H), 5.51 (d, 1H, $J = 8.8$ Hz), 4.11 (br s, 2H), 4.05 (t, 1H, $J = 8.0$ Hz), 3.56-3.52 (m, 1H), 3.42 (td, 1H, $J = 10.4, 3.2$ Hz), 2.60-2.39 (m, 3H), 1.94 (t, 2H, $J = 7.6$ Hz), 1.84-1.75 (m, 2H), 1.70-1.57 (m, 2H), 1.11 (d, 3H, $J = 6.8$ Hz), 0.94 (d, 3H, $J = 6.8$ Hz); ^{13}C NMR (100 MHz, C_6D_6) 142.3, 139.9, 130.0, 128.4, 128.3, 125.8, 71.9, 59.0, 35.9,

35.5, 33.9, 33.4, 29.8, 18.7, 18.4; IR (film) 3362, 2954, 1660, 1454, 1009 cm^{-1} ; HRMS (EI^+) calc'd for $[\text{C}_{17}\text{H}_{26}\text{O}_2]^+$: m/z 262.1933, found 262.1935; Anal calc'd for $\text{C}_{17}\text{H}_{26}\text{O}_2$: C, 77.82; H, 9.99; found: C, 77.76; H, 10.13; Enantiomeric purity was determined by chiral HPLC analysis, Chiralcel OD column, 99:1 hexanes:isopropanol, 1 mL/min; t_R 64.4 min (minor), 70.2 min (major): 90% ee.

Synthesis of Enol Ether **11**:

A solution of **SI-1** (1.47 g, 7.80 mmol) in THF (22 mL) was cooled to $-15\text{ }^{\circ}\text{C}$ and NaH (0.312 g, 7.80 mmol) was added. The resulting suspension was warmed to $-10\text{ }^{\circ}\text{C}$ over 15 min and a solution of **SI-2** (2.11 g, 7.80 mmol) in THF (5 mL) was added. The resulting dark red mixture was gradually warmed to rt and left to stir for 16 h. The reaction mixture was slowly quenched with H_2O (20 mL) and extracted with Et_2O (3x, 20 mL). The combined extracts were washed with brine (1x, 50 mL), dried over MgSO_4 , filtered, and concentrated. The crude mixture was purified by flash column chromatography (100:1 to 50:1 hexanes:EtOAc eluent) to afford the desired vinylogous carbonate (2.24 g, 63% yield, 5:1 *E:Z*, R_f = 0.82 in 3:1 hexanes:EtOAc) as a colorless oil: ^1H NMR (400 MHz, CDCl_3) The following were observed for the major alkene isomer δ 7.28-7.25 (m, 2H), 7.19-7.15 (m, 3H), 5.23 (s, 1H), 4.64 (q, 1H, J = 6.4 Hz), 4.16-4.03 (m, 2H), 3.65 (t, 2H, J = 6.8 Hz), 2.82-2.74 (m, 2H), 2.70 (t, 2H, J = 7.6 Hz), 2.20 (t, 2H, J = 6.8 Hz), 1.84-1.75 (m, 4H), 1.54 (d, 3H, J = 6.4 Hz), 1.21 (t, 3H, J = 7.2 Hz), 0.89 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) The following were observed for the major alkene isomer δ 173.7, 167.6, 141.5, 128.5, 128.3, 125.9, 92.9, 86.7, 78.7, 63.9, 62.9, 59.3, 34.6, 30.7, 30.0, 28.7, 26.0, 22.2, 18.4, 18.1, 14.4, -5.2 (2); IR (film) 2930, 2245, 1712, 1621, 1256 cm^{-1} ; HRMS (FAB^+) calc'd for $[\text{C}_{27}\text{H}_{42}\text{O}_4\text{Si} + \text{Li}]^+$: m/z 465.3012, found 465.3007; Anal calc'd for $\text{C}_{27}\text{H}_{42}\text{O}_4\text{Si}$: C, 70.70; H, 9.23; found: C, 70.32; H, 9.43.

A solution of **SI-3** (2.18 g, 4.75 mmol) in Et_2O (14 mL) was cooled to $-78\text{ }^{\circ}\text{C}$ and DIBAL-H (10.4 mL, 1.5 M in PhMe) was added dropwise. The resulting mixture was maintained at $-78\text{ }^{\circ}\text{C}$ for 1 h and quenched with an aqueous solution of Rochelle's salt (12 mL, 0.5 M). The mixture was warmed to rt and stirred vigorously for 2 h. The resulting mixture was extracted with Et_2O (3x, 20 mL) and the combined extracts washed with brine (1x, 25 mL), dried over MgSO_4 , filtered, and concentrated. The crude mixture was purified by flash column chromatography (1% TEA in 12:1 hexanes:EtOAc eluent) to afford the desired alcohol (1.42 g, 72% yield, R_f = 0.53 in 3:1 hexanes:EtOAc) as a colorless oil: ^1H NMR (500 MHz, CDCl_3) δ 7.30-7.26 (m, 2H), 7.20-7.17 (m, 3H), 5.09 (t, 1H, J = 8.0 Hz), 4.62 (q, 1H, J = 6.5 Hz), 4.16-4.08 (m, 2H), 3.70-3.61 (m, 2H), 2.71 (t, 2H, J = 7.5 Hz), 2.39-2.30 (m, 2H), 2.26 (br s, 1H), 2.20 (td, 2H, J = 7.0, 1.5 Hz), 1.81 (quintet, 2H, J = 7.0 Hz), 1.74-1.68 (m, 2H), 1.49 (d, 3H, J = 6.5 Hz), 0.91 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 158.0, 141.6, 128.5, 128.4, 125.9, 99.9, 85.3, 80.2, 62.2, 61.6, 58.6, 34.7, 30.2, 30.0, 25.9, 25.7, 22.5, 18.4, 18.1, -5.2 (2); IR (film) 3399, 2931, 1658, 1253, 1083 cm^{-1} ; HRMS (EI^+) calc'd for $[\text{C}_{25}\text{H}_{40}\text{O}_3\text{Si}]^+$: m/z 416.2747, found 416.2742; Anal calc'd for $\text{C}_{25}\text{H}_{40}\text{O}_3\text{Si}$: C, 72.06; H, 9.68; found: C, 71.92; H, 10.01.

Selected nOe cross peaks for alcohol **SI-4**

To a solution of **SI-4** (1.29 g, 3.10 mmol) in CH_2Cl_2 (9 mL) was added TEA (0.941 g, 1.30 mL, 9.30 mmol), Ac_2O (0.633 g, 0.58 mL, 6.20 mmol) and DMAP (5 mol%). The resulting solution was left to stir at rt 12 h and quenched with H_2O (10 mL). The mixture was extracted with Et_2O (3x, 10 mL) and the combined extracts washed with brine (1x, 15 mL), dried over MgSO_4 , filtered, and concentrated. The crude mixture was purified by flash column chromatography (1% TEA in 15:1 hexanes:EtOAc eluent) to afford the desired acetate (1.32 g, 93% yield, $R_f = 0.74$ in 3:1 hexanes:EtOAc) as a colorless oil: ^1H NMR (400 MHz, CDCl_3) δ 7.34-3.0 (m, 2H), 7.24-7.21 (m, 3H), 4.93 (t, 1H, $J = 8.0$ Hz), 4.68-4.61 (m, 3H), 3.65 (t, 2H, $J = 6.4$ Hz), 2.75 (t, 2H, $J = 7.6$ Hz), 2.32 (t, 2H, $J = 7.2$ Hz), 2.24 (td, 2H, $J = 7.2, 2.0$ Hz), 2.01 (s, 3H), 1.85 (quintet, 2H, $J = 7.2$ Hz), 1.79-1.73 (m, 2H), 1.54 (d, 3H, $J = 6.4$ Hz), 0.94 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.2, 160.5, 141.6, 128.6, 128.4, 125.9, 94.0, 85.5, 79.9, 62.6, 62.3, 61.5, 34.7, 30.9, 30.2, 26.7, 26.0, 22.4, 21.1, 18.3, 18.1, -5.3 (2); IR (film) 2932, 2241, 1739, 1659, 1225, 1084 cm^{-1} ; HRMS (EI^+) calc'd for $[\text{C}_{27}\text{H}_{42}\text{O}_4\text{Si}]^+$: m/z 458.2852, found 458.2857; Anal calc'd for $\text{C}_{27}\text{H}_{42}\text{O}_4\text{Si}$: C, 70.70; H, 9.23; found: C, 71.02; H, 9.40.

A solution of **SI-5** (0.500 g, 1.09 mmol) in THF (3.6 mL) was cooled to 0 °C and TBAF (1.14 mmol, 1.14 mmol, 1.0 M in THF) was added. The resulting mixture was left to stir for 4 h and quenched with H_2O (10 mL). The mixture was extracted with Et_2O (3x, 10 mL) and the combined extracts washed with brine (1x, 10 mL), dried over MgSO_4 , filtered, and concentrated. The crude mixture was purified by flash column chromatography (1% TEA in 3:1 hexanes:EtOAc eluent) to afford the desired alcohol (0.325 g, 87% yield, $R_f = 0.13$ in 3:1 hexanes:EtOAc) as a colorless oil: ^1H NMR (400 MHz, CDCl_3) δ 7.37-7.27 (m, 2H), 7.21-7.17 (m, 3H), 4.92 (t, 1H, $J = 8.4$ Hz), 4.69-4.59 (m, 3H), 3.65 (t, 2H, $J = 6.0$ Hz), 2.70 (t, 2H, $J = 7.6$ Hz), 2.35 (td, 2H, $J = 7.2, 2.4$ Hz), 2.20 (td, 2H, $J = 7.2, 1.6$ Hz), 2.10-2.00 (br s, 1H), 1.98 (s, 3H), 1.84-1.72 (m, 4H), 1.51 (d, 3H, $J = 6.8$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 171.2, 160.0, 141.5, 128.5, 128.3, 125.9, 94.5, 85.7, 79.6, 62.6, 61.5, 61.4, 34.6, 30.3, 30.1, 26.4, 22.3, 21.1, 18.0; IR (film) 3449, 2936, 2241, 1737, 1239, 1077 cm^{-1} ; Anal calc'd for $\text{C}_{21}\text{H}_{28}\text{O}_4$: C, 73.23; H, 8.19; found: C, 73.42; H, 8.52.

(R)-11

The crude mixture was purified by flash column chromatography (1% TEA in 3:1 hexanes:EtOAc eluent) to afford the desired vinyl ether (0.302 g, 91% yield, $R_f = 0.20$ in 3:1 hexanes:EtOAc) as a colorless oil: Spectral data were consistent with those described for ($\pm$)-**11**.

Synthesis of Dialdehyde 17:

A solution of **16** (61.7 mg, 0.371 mmol) in CD_2Cl_2 (1.24 mL) was added to AgSbF_6 (6.2 mg, 18 μmol), the reaction mixture was left to stir in the dark, and monitored by ^1H NMR. After 10.5 h no **16** was detected in the reaction mixture and the solution was filtered through a silica gel plug with 1:1 hexanes:EtOAc (20 mL). The filtrate was concentrated to afford the desired dialdehyde as a pale yellow oil (61.0 mg) which was used directly without further purification: ^1H NMR (500 MHz, CD_2Cl_2) δ 9.56 (t, 1H, $J = 2.5$ Hz), 9.34

(s, 1H), 5.42-5.37 (qt, 1H, $J = 7.0, 2.5$ Hz), 2.87 (td, 2H, $J = 2.5, 1.0$ Hz), 1.70 (d, 3H, $J = 7.0$ Hz), 1.16 (s, 6H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 205.1, 202.4, 199.8, 97.6, 90.6, 49.2, 43.1, 20.9 (2), 14.7.

References:

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Selected Analytical Data:

^1H NMR for aldehyde **3**

NOESY for pyran hemiacetal **8b**

NOESY for spiroketal **10a**

HMQC for spiroketal **10a**

HPLC trace for spiroketal (±)-12

1: 210 nm, 4 nm Results

Retention Time	Area	Area Percent
9.512	6295714	49.836
12.312	6337224	50.164

HPLC trace for spiroketal 12

1: 210 nm, 4 nm Results

Retention Time	Area	Area Percent
9.141	955184	8.900
12.037	9777390	91.100