2, 3, 4- or -2, 3, 5-Trisubstituted Furans, Where to Go? Catalyst-Controlled Highly Regioselectively Ring Opening Cycloisomerization Reaction of Cyclopropenyl Ketones.

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Supporting Information

(1) Cycloisomerization of 1-acetyl-2-butylcycloprop-2-enecarboxylic acid ethyl ester (1a).

Typical procedure (Conditions A): 2-Methyl-5-butylfuran-3-carboxylic acid ethyl ester (2a): PdCl₂(CH₃CN)₂ (6.5 mg, 5 mol%) was added to a solution of **1a** (105 mg, 0.5 mmol) in 2 mL of CHCl₃. The mixture was then stirred under reflux for 18 h. Evaporation and chromatography on silica gel (petroleum ether/diethyl ether 10:1) gave **2a** (75 mg, 71%) as a liquid. ¹H NMR (CDCl₃, 300 MHz): δ = 6.14 (s, 1 H), 4.19 (q, *J* = 7.3 Hz, 2 H), 2.47 (t, *J* = 7.3 Hz, 2 H), 2.45 (s, 3 H), 1.58-1.48 (m, 2 H), 1.38-1.18 (m, 2 H), 1.26 (t, *J* = 7.3 Hz, 3 H), 0.85 (t, *J* = 7.3 Hz, 3 H); ¹³C NMR (CDCl₃, 75.4 MHz): δ = 164.35, 157.40, 154.24, 113.67, 105.27, 59.82, 29.79, 27.26, 22.08, 14.29, 13.71, 13.62; MS (70 eV): *m/z* (%): 210 (45.43) [*M*⁺], 168 (100); IR (neat): 1717, 1619, 1587, 1232, 1085 cm⁻¹; HRMS calcd for C₁₂H₁₈O₃: 210.12560, found: 210.12392.

Typical procedure (Conditions B): 2-Methyl-4-butylfuran-3-carboxylic acid ethyl ester (3a): CuI (4.7 mg, 5 mol%) was added to a solution of **1a** (105 mg, 0.5 mmol) in 2 mL of CH₃CN. The mixture was then stirred at 80°C for 9 h. Evaporation and

chromatography on silica gel (petroleum ether/diethyl ether 10:1) afforded **3a** (96 mg, 91%) as a liquid. ^1H NMR (CDCl_3 , 300 MHz): δ = 7.01 (s, 1 H), 4.28 (q, J = 7.5 Hz, 2 H), 2.56 (t, J = 7.5 Hz, 2 H), 2.52 (s, 3 H), 1.54-1.42 (m, 2 H), 1.42-1.20 (m, 2 H), 1.34 (t, J = 7.5 Hz, 3 H), 0.89 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (CDCl_3 , 75.4 MHz): δ = 164.72, 160.12, 137.25, 126.24, 112.86, 59.76, 31.67, 24.44, 22.54, 14.41, 14.28, 13.92; MS (70 eV): m/z (%): 210 (45.34) [M^+], 168 (100); IR (neat): 1716, 1607, 1561, 1302, 1270, 1098 cm^{-1} ; HRMS calcd for $\text{C}_{12}\text{H}_{18}\text{O}_3$: 210.12560, found: 210.12613.

(2) Cycloisomerization of 1-acetyl-2-(2'-tert-butyltrimethyl)silanyloxyethyl-cycloprop-2-enecarboxylic ethyl ester (1b).

Conditions A: 2-Methyl-5-(2'-tert-butyltrimethyl)silanyloxyethylfuran-3-carboxylic acid ethyl ester (2b): The reaction of **1b** (156 mg, 0.5 mmol) and $\text{PdCl}_2(\text{CH}_3\text{CN})_2$ (6.5 mg, 5 mol%) in 4 mL of CH_2Cl_2 under reflux afforded **2b** (101 mg, 65%) as a liquid. ^1H NMR (CDCl_3 , 300 MHz) δ = 6.28 (s, 1 H), 4.24 (q, J = 7.2 Hz, 2 H), 3.81 (t, J = 7.2 Hz, 2 H), 2.76 (t, J = 7.2 Hz, 2 H), 2.51 (s, 3 H), 1.31 (t, J = 7.2 Hz, 3 H), 0.86 (s, 9 H), 0 (s, 6 H); ^{13}C NMR (CDCl_3 , 75.4 MHz) δ = 164.24, 157.65, 151.05, 113.87, 106.90, 61.35, 59.83, 31.48, 25.77, 18.20, 14.28, 13.60, -5.53; MS (70 eV): m/z (%): 313 (3.87) [$M^+ + 1$], 255 (100) [$M^+ - \text{C}_4\text{H}_9$]; IR (neat): 1718, 1620, 1587, 1257, 1083 cm^{-1} ; HRMS calcd for $\text{C}_{15}\text{H}_{25}\text{O}_4\text{Si}$ [$M^+ - \text{CH}_3$]: 297.15221, found: 297.15007.

Conditions B: 2-Methyl-4-(2'-tert-butyltrimethyl)silanyloxyethylfuran-3-carboxylic acid ethyl ester (3b): The reaction of **1b** (156 mg, 0.5 mmol) and CuI (5 mg, 5 mol%) in 2 mL of CH_3CN afforded **3b** (132 mg, 85%) as a liquid. ^1H NMR (CDCl_3 , 300 MHz) δ = 7.08 (s, 1 H), 4.26 (q, J = 6.9 Hz, 2 H), 3.75 (t, J = 6.6 Hz, 2 H), 2.79 (t, J = 6.6 Hz, 2 H), 2.50 (s, 3 H), 1.32 (t, J = 6.9 Hz, 3 H), 0.85 (s, 9 H), -0.02 (s, 6 H); ^{13}C NMR (CDCl_3 ,

75.4 MHz) δ = 164.47, 159.83, 138.46, 122.36, 112.82, 62.67, 59.73, 28.20, 25.83, 18.20, 14.31, 14.25, -5.45; MS (70 eV): m/z (%): 313 (8.22) [M^+ +1], 255 (100) [M^+ -C₄H₉]; IR (neat): 2957, 2931, 2859, 1717, 1607, 1562, 1100, 837, 777 cm⁻¹; HRMS calcd for C₁₆H₂₈O₄Si: 312.17569, found: 312.17514.

(3) Cycloisomerization of 1-acetyl-2-(*tert*-butyldimethyl)silanyloxymethylcycloprop-2-enecarboxylic acid ethyl ester (1c).

Conditions A: 2-Methyl-5-(*tert*-butyldimethyl)silanyloxymethylfuran-3-carboxylic acid ethyl ester (2c): The reaction of **1c** (100 mg, 0.34 mmol) and PdCl₂(CH₃CN)₂ (4.0 mg, 5 mol%) in 2 mL of CHCl₃ under reflux afforded **2c** (60 mg, 60%) as a liquid. ¹H NMR (CDCl₃, 300 MHz) δ = 6.45 (s, 1 H), 4.55 (s, 2 H), 4.26 (q, J = 7.2 Hz, 2 H), 2.54 (s, 3 H), 1.32 (t, J = 7.2 Hz, 3 H), 0.89 (s, 9 H), 0.07 (s, 6 H); ¹³C NMR (CDCl₃, 75.4 MHz) δ = 164.11, 158.82, 152.01, 113.95, 108.06, 60.00, 57.78, 25.82, 18.37, 14.31, 13.78, -5.27; MS (70 eV): m/z (%): 299 (4.02) [M^+ +1], 241 (100) [M^+ -C₄H₉]; IR (neat): 1726, 1677, 1599, 1268, 1241 cm⁻¹; HRMS calcd for C₁₄H₂₃O₄Si [M^+ -CH₃]: 283.13656, found: 283.13727.

Conditions B: 2-Methyl-4-(*tert*-butyldimethyl)silanyloxymethylfuran-3-carboxylic acid ethyl ester (3c): The reaction of **1c** (144 mg, 0.48 mmol) and CuI (5 mg, 5 mol%) in 2 mL of CH₃CN afforded **3c** (120 mg, 85%) as a liquid. ¹H NMR (CDCl₃, 300 MHz) δ = 7.18 (s, 1 H), 4.77 (d, J = 1.2 Hz, 2 H), 4.25 (q, J = 7.5 Hz, 2 H), 2.52 (s, 3 H), 1.32 (t, J = 7.5 Hz, 3 H), 0.91 (s, 9 H), 0.08 (s, 6 H); ¹³C NMR (CDCl₃, 75.4 MHz) δ = 164.33, 160.16, 137.81, 127.27, 111.40, 59.93, 58.71, 25.86, 18.34, 14.27, 14.19, -5.50; MS (70 eV): m/z (%): 298 (0.50) [M^+], 241 (100) [M^+ -C₄H₉]; IR (neat): 1718, 1613, 1567, 1259, 1095 cm⁻¹; HRMS calcd for C₁₁H₁₇O₄Si [M^+ -C₄H₉]: 241.08962, found: 241.08623.

(4) Cycloisomerization of 1-acetyl-2-(*tert*-butyl)cycloprop-2-enecarboxylic acid ethyl ester (1d**).**

Conditions A: 2-Methyl-5-(*tert*-butyl)furan-3-carboxylic acid ethyl ester (2d**):** The reaction of **1d** (105 mg, 0.5 mmol) and PdCl₂(CH₃CN)₂ (6.5 mg, 5 mol%) in 2 mL of CHCl₃ under reflux afforded **2d** (69 mg, 66%) as a liquid. ¹H NMR (CDCl₃, 300 MHz) δ = 6.18 (s, 1 H), 4.25 (q, *J* = 7.2 Hz, 2 H), 2.52 (s, 3 H), 1.32 (t, *J* = 7.2 Hz, 3 H), 1.24 (s, 9 H); ¹³C NMR (CDCl₃, 75.4 MHz) δ = 164.50, 162.04, 157.43, 113.42, 102.59, 59.86, 32.30, 28.78, 14.37, 13.73; MS (70 eV): *m/z* (%): 210 (12.60) [*M*⁺], 195 (100) [*M*⁺-CH₃]; IR (neat): 1718, 1615, 1580, 1255, 1233, 1071 cm⁻¹; HRMS calcd for C₁₂H₁₈O₃: 210.12560, found: 210.12649.

Conditions B: 2-Methyl-4-(*tert*-butyl)furan-3-carboxylic acid ethyl ester (3d**):** The reaction of **1d** (55 mg, 0.26 mmol) and CuI (2 mg, 5 mol%) in 1 mL of CH₃CN afforded **3d** (44 mg, 80%) as a liquid. ¹H NMR (CDCl₃, 300 MHz) δ = 6.99 (s, 1 H), 4.29 (q, *J* = 6.9 Hz, 2 H), 2.48 (s, 3 H), 1.38 (t, *J* = 6.9 Hz, 3H), 1.33 (s, 9 H); ¹³C NMR (CDCl₃, 75.4 MHz) δ = 164.95, 160.47, 136.17, 135.29, 113.11, 60.17, 30.74, 29.83, 14.99, 14.23; MS (70 eV): *m/z* (%): 210 (11.27) [*M*⁺], 149 (100) [*M*⁺-CH₃-EtOH]; IR (neat): 1812, 1779, 1721, 1277, 1090 cm⁻¹; HRMS calcd for C₁₂H₁₈O₃: 210.12560, found: 210.12506.

(5) Cycloisomerization of 1-acetyl-2-phenyl-cycloprop-2-enecarboxylic acid ethyl ester (1e**).**

Conditions A: 2-Methyl-5-phenylfuran-3-carboxylic acid ethyl ester (2e**):**¹ The reaction of **1e** (115 mg, 0.5 mmol) and PdCl₂(CH₃CN)₂ (6.5 mg, 5 mol%) in 2 mL of CHCl₃ under reflux afforded **2e**¹ (84 mg, 73%) as an oil. ¹H NMR (CDCl₃, 300 MHz) δ = 7.64 (d, *J* = 7.5 Hz, 2 H), 7.44-7.32 (m, 2 H), 7.30-7.24 (m, 1 H), 6.89 (s, 1 H), 4.32 (q,

$J = 7.2$ Hz, 2 H), 2.65 (s, 3 H), 1.38 (t, $J = 7.2$ Hz, 3 H); ^{13}C NMR (CDCl_3 , 75.4 MHz) $\delta = 163.99, 158.53, 151.59, 129.98, 128.63, 127.52, 123.52, 115.31, 105.40, 60.13, 14.31, 13.84$; MS (70 eV): m/z (%): 230 (87.30) [M^+], 201 (100) [$M^+ - \text{C}_2\text{H}_5$]; IR (neat): 1718, 1616, 1604, 1561, 1234, 1097 cm^{-1} .

Conditions B: 2-Methyl-4-phenylfuran-3-carboxylic acid ethyl ester (3e):² The reaction of **1e** (115 mg, 0.5 mmol) and CuI (4 mg, 5 mol%) in 2 mL of CH_3CN afforded **3e**² (102 mg, 89%) as an oil. ^1H NMR (CDCl_3 , 300 MHz) $\delta = 7.44\text{--}7.29$ (m, 5 H), 7.28 (s, 1 H), 4.11 (q, $J = 7.2$ Hz, 2 H), 2.62 (s, 3 H), 1.19 (t, $J = 7.2$ Hz, 3 H); ^{13}C NMR (CDCl_3 , 75.4 MHz) $\delta = 164.10, 160.12, 138.14, 131.92, 129.18, 127.67, 127.31, 127.20, 112.67, 59.95, 14.27, 13.93$; MS (70 eV): m/z (%): 230 (100) [M^+]; IR (neat): 1778, 1714, 1600, 1289, 1112, 1076 cm^{-1} .

(6) Cycloisomerization of 1-benzoyl-2-pentylcycloprop-2-enecarboxylic acid ethyl ester (1f).

Conditions A: 2-Phenyl-5-pentylfuran-3-carboxylic acid ethyl ester (2f): The reaction of **1f** (100 mg, 0.35 mmol) and $\text{PdCl}_2(\text{CH}_3\text{CN})_2$ (4.5 mg, 5 mol%) in 2 mL of CH_2Cl_2 under reflux afforded **2f** (50 mg, 50%) as an oil. ^1H NMR (CDCl_3 , 300 MHz) $\delta = 8.02\text{--}7.92$ (m, 2 H), 7.50–7.35 (m, 3 H), 6.45 (s, 1 H), 4.29 (q, $J = 6.9$ Hz, 2 H), 2.66 (t, $J = 7.5$ Hz, 2 H), 1.75–1.62 (m, 2 H), 1.48–1.30 (m, 4 H), 1.34 (t, $J = 6.9$ Hz, 3 H), 0.93 (t, $J = 6.9$ Hz, 3 H); ^{13}C NMR (CDCl_3 , 75.4 MHz) $\delta = 163.87, 155.76, 155.48, 130.13, 128.87, 128.13, 127.99, 114.29, 107.94, 60.34, 31.29, 27.71, 27.43, 22.38, 14.25, 13.98$; MS (70 eV): m/z (%): 286 (54.37) [M^+], 229 (100) [$M^+ - \text{C}_4\text{H}_9$]; IR (neat): 1720, 1557, 1492, 1209, 1102 cm^{-1} ; HRMS calcd for $\text{C}_{18}\text{H}_{22}\text{O}_3$: 286.15689, found: 286.15635.

Conditions B: 2-Phenyl-4-pentylfuran-3-carboxylic acid ethyl ester (3f): The reaction of **1f** (100 mg, 0.35 mmol) and CuI (4 mg, 6 mol%) in 2 mL of CH₃CN afforded **3e** (102 mg, 89%) as an oil. ¹H NMR (CDCl₃, 300 MHz) δ = 7.85-7.72 (m, 2 H), 7.50-7.32 (m, 3 H), 7.26 (s, 1 H), 4.31 (q, J = 7.5 Hz, 2 H), 2.65 (t, J = 6.6 Hz, 2 H), 1.68-1.50 (m, 2 H), 1.50-1.30 (m, 4 H), 1.31 (t, J = 7.5 Hz, 3 H), 0.94 (t, J = 7.2 Hz, 3 H); ¹³C NMR (CDCl₃, 75.4 MHz) δ = 164.49, 157.63, 138.74, 130.41, 128.89, 128.30, 127.87, 127.51, 113.62, 60.29, 31.70, 29.25, 24.73, 22.49, 14.04, 14.00; MS (70 eV): m/z (%): 286 (33.83) [M^+], 230 (100) [M^+ -C₄H₈]; IR (neat): 1716, 1594, 1545, 1488, 1294, 1208, 1085, 1066 cm⁻¹; HRMS calcd for C₁₈H₂₂O₃: 286.15689, found: 286.15808.

(7) Cycloisomerization of 1-acetyl-2-butyl-cycloprop-2-enyl methyl ketone (1g).

Conditions A: 2-Methyl-3-acetyl-5-butylfuran (2g): The reaction of **1g** (90 mg, 0.5 mmol) and PdCl₂(CH₃CN)₂ (6.5 mg, 5 mol%) in 4 mL of CH₂Cl₂ under reflux afforded **2g** (70 mg, 78%) as a liquid. ¹H NMR (CDCl₃, 300 MHz) δ = 6.10 (s, 1 H), 2.48 (t, J = 7.8 Hz, 2 H), 2.45 (s, 3 H), 2.28 (s, 3 H), 1.56-1.46 (m, 2 H), 1.35-1.22 (m, 2 H), 0.84 (t, J = 7.2 Hz, 3 H); ¹³C NMR (CDCl₃, 75.4 MHz) δ = 194.34, 156.69, 154.26, 121.85, 105.15, 29.83, 29.05, 27.25, 22.10, 14.28, 13.71; MS (70 eV): m/z (%): 180 (74.58) [M^+], 137 (100) [M^+ -C₃H₇]; IR (neat): 1679, 1607, 1572, 1399, 1232 cm⁻¹; HRMS calcd for C₁₁H₁₆O₂: 180.11503, found: 180.11448.

Conditions B: 2-Methyl-3-acetyl-4-butylfuran (3g): The reaction of **1g** (90 mg, 0.5 mmol) and CuI (5 mg, 5 mol%) in 2 mL of CH₃CN afforded **3g** (72 mg, 80%) as a liquid. ¹H NMR (CDCl₃, 300 MHz) δ = 6.98 (t, J = 0.9 Hz, 1 H), 2.55 (td, J = 7.5 and 0.9 Hz, 2 H), 2.50 (s, 3 H), 2.39 (s, 3 H), 1.55-1.42 (m, 2 H), 1.42-1.32 (m, 2 H), 0.89 (t, J = 7.2 Hz, 3 H); ¹³C NMR (CDCl₃, 75.4 MHz) δ = 194.67, 158.75, 137.32, 125.83, 122.00, 31.37,

30.75, 24.82, 22.48, 15.31, 13.82; MS (70 eV): m/z (%): 180 (21.25) [M^+], 43 (100) [$C_3H_7^+$]; IR (neat): 1775, 1670, 1587, 1549, 1409, 1118, 1071 cm^{-1} ; HRMS calcd for $C_{11}H_{16}O_2$: 180.11503, found: 180.11338.

(8) Cycloisomerization of 1-(phenylsulfonyl)-2-butylcycloprop-2-enyl methyl ketone (1h).

Conditions A: 2-Methyl-3-(phenylsulfonyl)-5-butylfuran (2h): The reaction of **1h** (139 mg, 0.5 mmol) and $PdCl_2(CH_3CN)_2$ (6.5 mg, 5 mol%) in 5 mL of CH_2Cl_2 under reflux afforded **2h** (123 mg, 88%) as colorless needles. m.p. 58-59 °C (Et_2O -hexane); 1H NMR ($CDCl_3$, 300 MHz) δ = 7.85-7.80 (m, 2 H), 7.52-7.36 (m, 3 H), 6.06 (s, 1 H), 2.45 (s, 3 H), 2.42 (t, J = 7.8 Hz, 2 H), 1.52-1.41 (m, 2 H), 1.30-1.20 (m, 2 H), 0.81 (t, J = 7.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ = 155.54, 154.72, 142.56, 132.85, 129.06, 126.64, 122.48, 104.39, 29.45, 27.19, 21.99, 13.59, 12.75; MS (70 eV): m/z (%): 278 (36.96) [M^+], 235 (100) [$M^+ - C_3H_7$]; IR (KBr): 1597, 1550, 1445, 1326, 1313, 1165 cm^{-1} ; Anal. calcd for $C_{15}H_{18}O_3S$: C, 64.72, H, 6.52, found: C, 64.83; H, 6.53.

Conditions B: 2-Methyl-3-(phenylsulfonyl)-4-butylfuran (3h): The reaction of **1g** (139 mg, 0.5 mmol) and CuI (5 mg, 5 mol%) in 2 mL of CH_3CN afforded **3g** (133 mg, 96%) as colorless needles. m.p. 59-60 °C (Et_2O -hexane); 1H NMR ($CDCl_3$, 300 MHz) δ = 7.90-7.82 (m, 2 H), 7.60-7.45 (m, 3 H), 7.02 (t, J = 0.9 Hz, 1 H), 2.62 (s, 3 H), 2.41 (td, J = 7.5 and 0.9 Hz, 2 H), 1.40-1.16 (m, 4 H), 0.77 (t, J = 7.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ = 158.20, 142.76, 137.91, 132.93, 129.03, 126.59, 124.63, 121.04, 30.69, 23.27, 22.36, 13.75, 13.65; MS (70 eV): m/z (%): 278 (11.75) [M^+], 236 (100) [$M^+ - C_3H_6$]; IR (KBr): 1602, 1574, 1467, 1445, 1307, 1151 cm^{-1} ; Anal. calcd for $C_{15}H_{18}O_3S$: C, 64.72, H, 6.52; found: C, 64.84; H, 6.80.

References:

- (1) Davies, H. M. L.; Romines, K. R. *Tetrahedron* **1988**, *44*, 3343.
- (2) Harigaya, Y.; Yamamoto, T.; Okawara, M. *Chem. Lett.* **1974**, 101.