Rhodium-Catalyzed Formylation of Organomercurials: Application to Efficient Polyol Synthesis

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Supporting Information

General Information. All reactions were conducted under an atmosphere of nitrogen in flame-dried glassware with magnetic stirring unless otherwise indicated. Rh(acac)$(CO)_2$ was purchased from Strem and was used as received. P(O-*o*-*t*-BuPh)$_3$ was prepared by the method of Van Leeuwen.[1] 1,4-diazabicyclo[2.2.2]octane (DABCO) was purchased from Aldrich and used as received. EtOAc was distilled from CaH_2 immediately prior to use. Infrared spectra were recorded on a Perkin Elmer Paragon 1000 FT-IR spectrometer. ^{1}H NMR spectra were recorded on a Varian VXR-200 (200 MHz) spectrometer, a Bruker DRX-300WB (300 MHz) spectrometer and a Bruker DMX-500 (500 MHz) spectrometer and are reported in ppm from internal tetramethylsilane. Data are reported as follows: (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet; coupling constant(s) in Hz; integration; assignment). Proton decoupled ^{13}C NMR spectra were recorded on a Varian VXR-300 (75 MHz) spectrometer using $CDCl_3$ (77.0 ppm) or C_6D_6 (128.0 ppm) as internal standard. ^{199}Hg spectra were recorded on a a Bruker DRX-300WB (300 MHz) spectrometer, frequency for ^{199}Hg, 53.7 MHz: pulse, 4.25 μsec; acquisition time, 0.5 sec; delay μsec; 5000- 20,000 scans. Calibration was made with $Hg(OAc)_2$ in 1M HOAc (0.5M) at -2389 ppm.[2] High resolution mass spectra were obtained on a JEOL HX110 mass spectrometer in the Columbia University Mass Spectrometry Laboratory.

General procedure for the rhodium-catalyzed formylation of organomercury chlorides. An oven-dried stainless steel pressure vessel equipped with a glass liner and magnetic stirring bar is charged with the organomercury chloride[3] and EtOAc to a concentration of 0.50 M. DABCO (0.50 equiv) is then added followed by P(O-*o*-*t*-BuPh)$_3$ (4 mol%) and Rh(acac)$(CO)_2$ (4 mol%). The bomb/pressure guage is assembled and the apparatus is pressurized to 500 psi with 1/1 H_2/CO and then vented. This procedure is repeated twice and the apparatus is then pressurized to 800 psi. The apparatus is heated by immersion in an oil bath set at 50 °C with magnetic stirring. After 6-18 h,[4] the apparatus is cooled in an ice bath and then vented. The reaction mixture is filtered through a pad of celite using generous amounts of CH_2Cl_2 for elution. The filtrate is concentrated and treated with pentane, and the mixture is cooled to 0 °C and filtered through a pad of celite using cold pentane for elution. The filtrate is concentrated and the residue is purified by chromatography on silica gel.

CAUTION! The reaction produces Hg and possibly Hg(II) salts as byproducts. These are removed in the filtrations and proper precautions should be taken during the workup to avoid exposure to these toxic substances.

Characterization data for aldehyde 2 (Table 1) and the aldehyde products in Table 2.

***cis-cis*-2-ethyl-6-octyl-4-(2-oxoethyl)-1,3-dioxane (2)**. ^{1}H NMR (300 MHz, CDCl$_3$) δ 9.81 (t, *J* = 2.0 Hz, 1H, C**H**O), 4.48 (t, *J* = 5.3 Hz, 1H, C(2)**H**), 4.16 (m, 1H, C(4)**H**), 3.58 (m, 1H, C(6)**H**), 2.68 (ddd, *J* = 2.2, 7.5, 16.7 Hz**,** 1H, one of C(4)-C**H**$_2$-CHO), 2.54 (ddd, *J* = 1.7, 5.0, 16.7 Hz**,** 1H, one of C(4)-C**H**$_2$-CHO), 1.3-1.4 (m, 4H, C(2)-C**H**$_2$CH$_3$, C(5)**H**$_2$), 0.86-0.94 (m, 14H, C(6)-(C**H**$_2$)$_7$), 0.89 (m, 6H, C(2)-CH$_2$C**H**$_3$, C(6)-(CH$_2$)$_7$C**H**$_3$); ^{13}C NMR (300 MHz, CDCl$_3$) δ 200.8, 102.8, 76.2, 71.4, 49.5, 36.8, 35.8, 31.9, 29.5, 29.3, 28.0, 25.0, 22.7, 14.1, 8.5; IR (thin film) 2919, 2859, 2719, 1727, 1462, 1378, 1343, 1343, 1148, 1123, 1029, 974, 869, 719 cm^{-1}; HRMS (FAB+) calc'd for $C_{16}H_{31}O_3$: 271.2273, found 271.2284.

***cis-cis*-2-ethyl-4-(2-oxoethyl)-6-pentyl-1,3-dioxane (Table 2, entry 1).** ^{1}H NMR (300 MHz, CDCl$_3$) δ 9.81 (t, *J* = 2.0 Hz, 1H, C**H**O), 4.48 (t, *J* = 5.3 Hz, 1H, C(2)**H**), 4.15 (m, 1H, C(4)**H**), 3.59 (m, 1H, C(6)**H**), 2.69 (ddd, *J* = 2.2, 7.5, 16.7 Hz, 1H, one of C(4)-C**H**$_2$-CHO), 2.55 (ddd, *J* = 1.7, 5.1, 16.7 Hz, 1H, one of C(4)-C**H**$_2$-CHO), 1.54-1.67 (m, 4H, C(2)-C**H**$_2$CH$_3$, C(5)**H**$_2$), 1.24-1.44 (m, 8H, C(6)-(C**H**$_2$)$_4$), 0.86-0.94 (m, 6H, C(2)-CH$_2$C**H**$_3$, C(6)-(CH$_2$)$_4$C**H**$_3$); ^{13}C NMR (300 MHz, CDCl$_3$) δ 200.8, 102.8, 76.2, 71.3, 49.5, 36.8, 35.8, 31.7, 28.0, 24.7, 22.6, 14.0, 8.5; IR (thin film) 2936, 2856, 2732, 1728, 1466, 1377, 1346, 1306, 1142, 1116, 1031, 983, 872 cm^{-1}; HRMS (EI) $[M-H]^+$ calc'd for $C_{13}H_{23}O_3$: 277.1647, found 227.1653.

***cis-cis*-6-Benzyloxymethyl-2-ethyl-4-(2-oxoethyl)-1,3-dioxane (Table 2, entry 2).** ^{1}H NMR (300 MHz, CDCl$_3$) δ 9.8 (t, *J* = 1.7 Hz, 1H, C**H**O), 7.33 (m, 5H, C$_6$**H**$_5$), 4.58 (d, *J* = 4.0 Hz, 2H, C**H**$_2$Ph), 4.54 (t, *J* = 5.3 Hz, 1H, C(2)**H**), 4.19 (m, 1H, C(4)**H**), 3.91 (m, 1H, C(6)**H**), 3.55 (dd, *J* = 6 and 10 Hz, 1H, one of C**H**$_2$OBn), 3.48 (dd, *J* = 4.6 and 10 Hz, 1H, one of C**H**$_2$OBn), 2.7 (ddd, *J* = 2.2, 7.5, 16.7 Hz, 1H, one of C(4)-C**H**$_2$-CHO), 2.56 (ddd, *J* = 1.5, 5.0, 16.7 Hz, 1H, one of C(4)-C**H**$_2$-CHO), 1.58-1.7 (m, 3H, one of C(2)-C**H**$_2$CH$_3$, C(5)-**H**$_2$), 1.43 (m, 1H, one of C(2)-C**H**$_2$CH$_3$), 0.93 (t, *J* = 7.5 Hz, 3H, C(2)-CH$_2$C**H**$_3$); ^{13}C NMR (300 MHz, CDCl$_3$) δ 200.5, 138, 128.4, 127.7, 102.7, 75.3, 73.5, 72.6, 71.1, 49.4, 33.3, 27.9, 8.4; IR (thin film)

3029, 2960, 2862, 2813, 2724, 1725, 1494, 1450, 1376, 1342, 1111, 974, 743, 699 cm^{-1}; HRMS (FAB+) calc'd for $C_{16}H_{22}O_4K$: 317.1155, found 317.1165.

***cis-cis*-6-(2-*tert*-Butyldimethylsilyloxy)ethyl-2-ethyl-4-(2-oxoethyl)-1,3-dioxane (Table 2, entry 3).** ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.81(t, *J* = 2.0 Hz, 1H, C**H**O), 4.49 (t, *J* = 5.3 Hz, 1H, C(2)**H**), 4.19 (m, 1H, C(4)**H**), 3.65- 3.82 (m, 3H, C(6)-C$\mathbf{H}_2$OTBS, C(6)**H**), 2.71 (ddd, *J* = 2.3, 7.6, 16.7 Hz, 1H, one of C(4)-C$\mathbf{H}_2$-CHO), 2.55 (ddd, *J* = 1.7, 4.9, 16.7 Hz, 1H, one of C(4)-C$\mathbf{H}_2$-CHO), 1.57-1.78 (m, 4H, C(6)-C$\mathbf{H}_2$CH_2OTBS, C(5)$\mathbf{H}_2$), 1.25 (m, 2H, **C**(2)-C$\mathbf{H}_2$CH_3), 0.89- 0.94 (m, 12 H, C(2)-CH_2C$\mathbf{H}_3$, OSiC(C$\mathbf{H}_3$)$_3$(CH_3)$_2$), 0.05 (s, 6H, SiC(CH_3)$_3$(C$\mathbf{H}_3$)$_2$); ^{13}C NMR (300 MHz, $CDCl_3$) δ 200.7, 102.8, 72.6, 71.4, 58.7, 49.4, 38.8, 36.9, 28.7, 28.0. 25.9, 8.6, -5.4; IR (thin film) 2919, 2859, 1727, 1462, 1383, 1348, 1253, 1138, 1098, 979, 839, 774 cm^{-1}; HRMS (FAB+) calc'd for $C_{16}H_{33}O_4Si$: 317.2148, found 317.2161.

***cis-cis*-2-ethyl-6-((*E)*-3-methyl-1-butenyl)-4-(2-oxoethyl)-1,3-dioxane (Table 2, entry 4).** ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.82 (t, *J* = 1.9 Hz, 1H, C**H**O), 5.66 (dd, *J* = 5.8 and 15.6 Hz, 1H, C(6)-C**H**=CH), 5.45 (ddd, *J* = 1.1, 6.2, 15.6 Hz,1H, C(6)-CH=C**H**CH(CH_3)$_2$), 4.55 (t, *J* = 5.2 Hz, 1H, C(2)**H**), 4.14 (m, 2H, C(4)**H**, C(6)**H**), 2.7 (ddd, *J* = 2.1, 7.4, 16.8 Hz**,** 1H, one of C(4)-C$\mathbf{H}_2$-CHO), 2.57 (ddd, *J* = 1.6, 5.1, 16.7 Hz, 1H, one of C(4)-C$\mathbf{H}_2$-CHO), 2.28 (m, 1 H, C(6)-CH=CHC**H**(CH_3)$_2$), 1.4-1.7 (m, 4H, C(2)-C$\mathbf{H}_2$CH_3, C(5)$\mathbf{H}_2$), 1.0 (d, *J* = 6.2 Hz, 6H, C(6)-CH=CHCH(C$\mathbf{H}_3$)$_2$), 0.93 (t, *J* = 7.5 Hz, 3H, C(2)-CH_2C$\mathbf{H}_3$); ^{13}C NMR (300 MHz, $CDCl_3$) δ 200.6, 139.8, 126.4, 102.6, 76.7, 71.1, 49.3, 36.9, 30.6, 28.0, 22.0, 8.4; IR (thin film) 2954, 2856, 2723, 1728, 1462, 1373, 1337, 1306, 1258, 1240, 1133, 1027, 974, 916, 867, 734 cm^{-1}; HRMS (EI) $[M-H]^+$ calc'd for $C_{13}H_{21}O_3$: 225.1491, found 225.1491.

***cis-cis*-5,5-dimethyl-2-ethyl-4-(2-oxoethyl)-6-pentyl-1,3-dioxane (Table 2, entry 5).** ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.80 (t, *J* = 2.1 Hz, 1H, C**H**O), 4.45 (t, *J* = 5.2 Hz, 1H, C(2)**H**), 3.84 (dd, *J* = 2.6 and 10 Hz, 1H, C(4)**H**), 3.21 (dd, *J* = 2.6 and 9.1 Hz, 1H, C(6)**H**), 2.56 (ddd, *J* = 2.5, 10, 16.2 Hz**,** 1H, one of C(4)-C$\mathbf{H}_2$-CHO), 2.45 (dt, *J* = 2.2 and 16.2 Hz**,** 1H, one of C(4)-C$\mathbf{H}_2$-CHO), 1.3-1.6 (m, 10H, C(2)-C$\mathbf{H}_2$CH_3, C(6)-(C$\mathbf{H}_2$)$_4$), 0.89 (m, 9H, C(2)-CH_2C$\mathbf{H}_3$, C(6)-(CH_2) $_4$C$\mathbf{H}_3$, C(5)-C$\mathbf{H}_3$), 0.73 (s, 3H, C(5)-C$\mathbf{H}_3$); ^{13}C NMR (300 MHz, $CDCl_3$) 201.9, 103.3, 85.5, 80.3, 43.3, 35.2, 31.8, 28.8, 27.8, 26.3, 22.6, 20.6, 14.1, 13.9, 8.4; IR (thin film) 2918, 2865, 2714, 1728, 1466, 1408, 1391, 1368, 1346, 1311, 1173, 1133, 1102, 1036, 983 cm^{-1}; HRMS (EI) $[M-H]^+$ calc'd for $C_{15}H_{27}O_3$: 255.1960, found 255.1954.

Characterization data for 9, 10, 11, 12, 13 and 14 (Scheme 5).

(4*R*,6*R*)-4-chloromercurymethyl-2,2-dimethyl-6-pentyl-1,3-dioxane (9). $[\alpha]_D^{22}$= -24.6 (*c* 0.976, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.25 (m, 1H, C(4)**H**), 3.81 (m, 1H, C(6)**H**), 2.28 (dd, *J* = 5.0, 11.9 Hz**,** 1H, one of C(4)-C**H**$_2$), 2.08 (dd, *J* = 5.9, 11.9 Hz**,** 1H, one of C(4)-C**H**$_2$), 1.0-1.7 (m, 16H, C(2)-(C**H**$_3$)$_2$, C(5)**H**$_2$, C(6)-(C**H**$_2$)$_4$), 0.89 (t, *J* = 6.3, 3H, C(6)-(CH$_2$)$_4$C**H**$_3$); ^{13}C NMR (300 MHz, $CDCl_3$) δ 98.8, 68.7, 67.9, 41.1, 39.6, 36.2, 31.7, 30.4, 24.6, 22.6, 20.1, 14.0; IR ($CDCl_3$) 2991, 2932, 2861, 1462, 1377, 1261, 1200, 1176, 1119, 1017, 926, 871, 733 cm^{-1}; HRMS (FAB+) $[M+H]^+$ calc'd for $C_{12}H_{24}O_2Hg^{202}Cl^{35}$: 437.1163, found 437.1155.

(4*S*,6*R*)-2,2-dimethyl-4-(2-oxoethyl)-6-pentyl-1,3-dioxane (10). $[\alpha]_D^{22}$= -154 (*c* 0.847, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.79 (t, *J* = 1.8 Hz, 1H, C**H**O), 4.90 (m, 1H, C(4)**H**), 3.85 (m, 1H, C(6)**H**), 2.58 (ddd, *J* = 2.2, 7.2, 16.6 Hz**,** 1H, one of C(4)-C**H**$_2$), 2.50 (ddd, *J* = 1.6, 5.1, 16.6 Hz**,** 1H, one of C(4)-C**H**$_2$), 1.1-1.7 (m, 16H, C(2)-(C**H**$_3$)$_2$, C(5)**H**$_2$, C(6)-(C**H**$_2$)$_4$), 0.89 (t, *J* = 6.3, 3H, C(6)-(CH$_2$)$_4$C**H**$_3$); ^{13}C NMR (300 MHz, $CDCl_3$) δ 201, 98.7, 68.8, 64.7, 49.9, 36.7, 36.3, 31.7, 30.0, 24.5, 22.6, 19.7, 14.0; IR (thin film) 2989, 2927, 2862, 2728, 1731, 1466, 1435, 1381, 1352, 1264, 1201, 1169, 1150, 1111, 1018, 998, 948, 874, 829, 727 cm^{-1}; HRMS (FAB+) $[M+H]^+$ calc'd for $C_{13}H_{25}O_3$: 229.1804, found 229.1814.

(4*S*,6*S*,8*R*)-6,8-bis-*O*-(1-methylethylidene)-1-tridecene-4,6,8-triol (11). $[\alpha]_D^{22}$= -7.67 (*c* 1.373, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.8 (m, 1H, C(2)**H**), 5.1 (m, 2 H, C(1)**H**$_2$), 4.1 (m, 1H, C(4)**H**), 3.9 (m, 2H, C(6)**H**, C(8)**H**), 3.5 (s, 1H, C(4)-O**H**), 2.2 (m, 2H, C(3)**H**$_2$), 1.1-1.6 (m, 18H, C(7)**H**$_2$, C(8)-(C**H**$_2$)$_4$, C(C**H**$_3$)$_2$, C(5)**H**$_2$), 0.88 (t, *J* = 6.6 Hz, 3H, C(13)**H**$_3$); ^{13}C NMR (300 MHz, $CDCl_3$) δ 134.9, 117.3, 98.6, 71.0, 70.3, 68.9, 42.3, 42.0, 37.1, 36.3, 31.7, 30.2, 24.6, 22.6, 19.9, 14.0; IR (thin film) 3466, 3077, 2993, 2937, 28, 1642, 1466, 1434, 1381, 1352, 1316, 1264, 1201, 1112, 996, 941, 915, 875, 823, 782 cm^{-1}; HRMS (FAB+) $[M+H]^+$ calc'd for $C_{16}H_{31}O_3$: 271.2273, found 271.2279.

(2*R*,4*R*,6*R*,8*R*)-1-chloromercury-2,4:6,8-bis-*O*-(1-methylethylidene)-tridecane-2,4,6,8-tetrol (12). $[\alpha]_D^{22}$= -16.0 (*c* 0.433, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.27 (m, 1H, C(2)**H**), 4.01 (m, 2H, C(4)**H**, C(6)**H**), 3.8 (m, 1H, C(8)**H**), 2.29 (dd, *J* = 4.9, 11.9 Hz**,** 1H, one of C(1)**H**$_2$), 2.06 (m, 1H, one of C(1)**H**$_2$), 1.0-1.8 (m, 26H, C(3)**H**$_2$, C(5)**H**$_2$, C(7)**H**$_2$, C(8)-(C**H**$_2$)$_4$, (C(C**H**$_3$)$_2$)$_2$), 0.89 (m, 3H, C(13)**H**$_3$); ^{13}C NMR (300 MHz, $CDCl_3$) δ 98.9, 98.3, 69.0, 67.9, 65.2, 65.0, 42.4, 40.8, 39.6, 36.7, 36.4, 31.8, 30.3, 29.9, 24.6, 22.6, 20.2, 19.8, 14.0; IR (CDCl$_3$) 2992, 2936, 2864, 2241, 1724, 1463, 1437, 1380, 1262, 1199, 1172, 1112, 1019, 970, 872, 735 cm^{-1}; HRMS (FAB+) [M-Cl]$^+$ calc'd for $C_{19}H_{35}O_4Hg^{202}$: 529.2245, found 529.2233.

(3*S*,5*S*,7*R*,9*R*)-3,5:7,9-bis-*O*-(1-methylethylidene)-1-tetradecanal-3,5,7,9-tetrol (13). [α]$_D^{23}$= -0.44 (*c* 0.503, CH$_2$Cl$_2$); ^{1}H NMR (300 MHz, CDCl$_3$) δ 9.79 (s, 1H, C**H**O), 4.40 (m, 1H, C(3)**H**), 4.06 (m, 2H, C(5)**H**, C(7)**H**), 3.80 (m, 1H, C(9)**H**), 2.59 (ddd, *J* = Hz, 1H, one of C(2)**H**$_2$), 2.50 (dd, *J* = Hz, 1H, one of C(2)**H**$_2$), 1.1-1.9 (m, 26H, C(4)**H**$_2$, C(6)**H**$_2$, C(8)**H**$_2$, (C(C**H**$_3$)$_2$)$_2$, C(9)-(C**H**$_2$)$_4$), 0.89 (t, *J* = 6.1 Hz, 3H, C(14)**H**$_3$); ^{13}C NMR (300 MHz, CDCl$_3$) δ 201, 98.7, 98.3, 68.9, 65.1, 65.0, 64.6, 49.8, 42.5, 36.7, 36.4, 36.3, 31.8, 30.2, 24.6, 22.6, 19.8, 19.7, 14.0; IR (thin film) 2993, 2940, 2728, 1732, 1465, 1436, 1380, 1263, 1200, 1017, 943, 874, 835, 734, 647, 523 cm^{-1}; HRMS (FAB+) [M-H]$^+$ calc'd for $C_{20}H_{35}O_5$: 355.2484, found 355.2482.

(4*S*,6*S*,8*S*,10*R*,12*R*)-6,8:10,12-bis-*O*-(1-methylethylidene)-1-heptadecene-4,6,8,10,12-pentaol (14). [α]$_D^{21}$= -6.83 (*c* 0.473, CH$_2$Cl$_2$); ^{1}H NMR (400 MHz, CDCl$_3$) δ 5.83 (m, 1H, C(2)**H**), 5.07 (m, 2 H, C(1)**H**$_2$), 3.78- 4.25 (m, 5H, C(4)**H**, C(6)**H**, C(8)**H**, C(10)**H**, C(12)**H**,), 3.50 (s, 1H, C(4)-O**H**), 2.16- 2.29 (m, 2H, C(3)**H**$_2$), 1.78 (ddd, *J* = 7.09 and 13.9 Hz, 1H, one of C(9)**H**$_2$), 1.00-1.64 (m, 27H, C(5)**H**$_2$, C(7)**H**$_2$, C(11)**H**$_2$, one of C(9)**H**$_2$, (C(C**H**$_3$)$_2$)$_2$, C(12)-(C**H**$_2$)$_4$), 0.89 (t, *J* = 6.6 Hz, 3H, C(17)**H**$_3$); ^{13}C NMR (300 MHz, CDCl$_3$) δ 134.8, 117.4, 98.6, 98.3, 71.0, 70.3, 68.9, 65.2, 42.5, 42.2, 41.96, 36.8, 36.7, 36.4, 31.8, 30.3, 30.2, 24.6, 22.6, 19.9, 19.8, 14.0; IR (CDCl$_3$) 3502, 2991, 2937, 2861, 1463, 1430, 1381, 1261, 1202, 1169, 1109, 935, 919, 870, 810 cm^{-1}; HRMS (FAB+) [M-H]$^+$ calc'd for $C_{23}H_{41}O_5$: 397.2954, found 397.2938.

***Tolypothrix* pentaether (7)**. The conversion of compound **14** to the natural product **7** was carried out according to the method of Brückner.[5] Complete experimental and spectral details are provided in that work. Our synthetic material was identical in every respect.

(1) Jongsma, T.; Challa, G.; Van Leeuwen, P. W. N. M. *J. Organomet. Chem.* **1991**, *421*, 121-128.

(2) Harris, R.K.; Mann, B.E. In *NMR and The Periodic Table*; Academic Press: New York, 1978; p 268.

(3) Sarraf, S. T.; Leighton, J. L. *Org. Lett.* **2000**, *2*, 403-405.

(4) The usual reaction time is 6 h. However, for more hindered substrates (*e.g.* entry 5, Table 2, and acetonides **7** and **10**) longer reaction times are necessary.

(5) Allerheiligen, S.; Brückner, R. *Liebigs Ann.* **1997**, 1667-1676.