Oxymercuration of Homoallylic Alcohol-Derived Hemiacetals: Diastereoselective Synthesis of Protected 1,3-Diols

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Supporting Information

General Information. All reactions were conducted under an atmosphere of nitrogen in flame-dried glassware with magnetic stirring. $Hg(OAc)_2$ (98+%) was purchased from Aldrich and used as received. Propionaldehyde was distilled prior to use. Infrared spectra were recorded on a Perkin Elmer Paragon 1000 FT-IR spectrometer. ^1H 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. High resolution mass spectra were obtained on a JEOL HX110 mass spectrometer in the Columbia University Mass Spectrometry Laboratory.

Preparation of HgClOAc: To a suspension of 12.7 g (40.0 mmol) of $Hg(OAc)_2$ in 10 mL of benzene was added 40.0 mL (40.0 mmol, 1.0 M in H_2O) of HCl. The mixture was stirred for 1 h, at which point it had become largely, but not completely, homogeneous. The mixture was warmed to 50 °C for 1 h, at which point it had become clear and homogeneous. The mixture was concentrated and dried under vacuum with heating to give a white powder: mp 146-151 °C, lit.[1] mp 145-149 °C.

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(1) Bowmaker G. A.; Churakov, A. V.; Harris, R. K.; Oh, S.-W. *J. Organomet. Chem.* **1998**, *550*, 89-99.

General Procedure, Method A, Table 1: To a mixture of 79.7 mg (0.250 mmol) $Hg(OAc)_2$ and 0.054 mL (0.750 mmol) propionaldehyde at -78 °C is added dropwise 0.250 mmol of homoallylic alcohol. The reaction mixture is allowed to warm to room temperature over the course of 1-2 hours at which time it becomes homogeneous. After addition of 10 mL of EtOAc and 5 mL of brine, the mixture is stirred for one hour. The organic layer is separated and the aqueous layer is extracted with 3 x 10 mL EtOAc. The combined organic extracts are dried ($MgSO_4$), filtered and concentrated. The residue is purified by chromatography on silica gel using CH_2Cl_2:hexane.

General Procedure, Method B, Table 1: To a mixture of 73.8 mg (0.250 mmol) HgClOAc and 0.054 mL (0.750 mmol) propionaldehyde at -78 °C is added dropwise 0.250 mmol of homoallylic alcohol. The reaction mixture is allowed to warm to room temperature over the course of 1-2 hours at which time it becomes homogeneous. The mixture is concentrated and the residue is purified by chromatography on silica gel using CH_2Cl_2:hexane.

In certain cases (entry 1, Table 1) the homoallylic alcohol freezes at –78 °C. In such cases the initial reaction temperature is raised to –35 °C.

***cis-cis*-4-Chloromercurymethyl-2-ethyl-6-octyl-1,3-dioxane (entry 1, Table 1):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.47 (t, *J* = 5.2 Hz, 1H, C(2)-**H**), 3.93 (m, 1H, C(4)-**H**), 3.54 (m, 1H, C(6)-**H**), 2.30 (dd, *J* = 5 and 12 Hz, 1H, one of C(4)-C**H**$_2$), 2.07 (dd, *J* = 7 and 12 Hz, 1H, one of C(4)-C**H**$_2$), 1.5-1.7 (m, 4H, C(2)-C**H**$_2$CH$_3$, C(5)-**H**$_2$), 1.1-1.4 (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 102.6, 76.1, 74.7, 41.0, 38.5, 35.8, 31.9, 29.5, 29.2, 28.1, 25.0, 22.7, 14.1, 8.0; IR (CH_2Cl_2) 2923, 2855, 2733, 1466, 1374, 1342, 1307, 1243, 1132, 1089, 1031, 970, 910, 868, 796, 722, 669 cm^{-1}; HRMS (FAB+) calcd for $C_{15}H_{28}ClHgO_2$: 473.1445, found 473.1423.

***cis-cis*-6-Benzyloxymethyl-4-chloromercurymethyl-2ethyl-1,3-dioxane (entry 2, Table 1):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (m, 5H, C$_6$**H**$_5$), 4.57-4.63 (d, *J* = 16.0 Hz, 2H, C**H**$_2$Ph), 4.53 (t, *J* = 5.2 Hz, 1H, C(2)-**H**), 4.00 (m, 1H, C(4)-**H**), 3.85 (m, 1H, C(6)-**H**), 3.57 (dd, *J* =

6 and 10 Hz, 1H, one of C**H**$_2$OBn), 3.45 (dd, *J* = 4.7 and 10 Hz, 1H, one of C(4)-C**H**$_2$OBn), 2.30 (dd, *J* = 5 and 12 Hz, 1H, one of C(4)-C**H**$_2$), 2.07 (dd, *J* = 6.9 and 12 Hz, 1H, one of C(4)-C**H**$_2$), 1.61-1.73 (m, 3H, one of C(2)-C**H**$_2$CH$_3$, C(5)-**H**$_2$), 1.3 (m, 1H, one of C(2)-C**H**$_2$CH$_3$), 0.94 (t, *J* = 7.5 Hz, 3H, C(2)-CH$_2$C**H**$_3$); ^{13}C NMR (300 MHz, $CDCl_3$) δ128.4, 127.8, 127.7, 102.5, 75.2, 74.5, 73.5, 72.6, 38.4, 37.5, 28.0, 8.5; IR (CH_2Cl_2) 2962, 2931, 2863, 1496, 1466, 1454, 1364, 1344, 1309, 1125, 1029, 972, 910, 866, 737 cm^{-1}; HRMS (FAB+) calcd for $C_{15}H_{21}ClHgO_3K$: 521.0484, found 521.0478.

***cis-cis*-6-(2-*tert*-Butyldimethylsilyloxy)ethyl-4-chloromercurymethyl-2ethyl-1,3-dioxane (entry 3, Table 1):**

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.48 (t, *J* = 5.2 Hz, 1H, C(2)-**H**), 3.97 (m, 1H, C(4)-**H**), 3.76 (m, 2H, C(6)-C**H**$_2$OTBS), 3.68 (m, 1H, C(6)-**H**), 2.30 (dd, *J* = 5 and 12 Hz, 1H, one of C(4)-C**H**$_2$), 2.07 (dd, *J* = 6.9 and 12 Hz, 1H, one of C(4)-C**H**$_2$), 1.58-1.74 (m, 4H, C(6)-C**H**$_2$CH$_2$OTBS, C(5)-**H**$_2$), 1.25 (m, 2H, C(2)-C**H**$_2$CH$_3$), 0.93 (t, *J* = 7.5 Hz, 3H, C(2)-CH$_2$C**H**$_3$), 0.89(s, 9H, OSiC(C**H**$_3$)$_3$(CH$_3$)$_2$), 0.05 (s, 6H, OSiC(CH$_3$)$_3$(C**H**$_3$)$_2$); ^{13}C NMR (300 MHz, $CDCl_3$) δ 102.5, 74.7, 72.5, 58.7, 41.0, 38.8, 38.5, 29.7, 28.0, 25.9, 18.3, 8.6, -5.4; IR (thin film) 2935, 2856, 2738, 1466, 1407, 1384, 1360, 1344, 1254, 1108 cm^{-1}; HRMS (FAB+) calcd for $C_{15}H_{31}ClHgO_3SiK$: 559.1035, found 559.1034.

***cis-cis*-4-Chloromercurymethyl-2-ethyl-6-(2-propenyl)-1,3-dioxane (entry 4, Table 1):**

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.76-5.86 (m, 1H, C(6)-CH$_2$C**H**=CH$_2$), 5.06-5.13 (m, 1H, C(6)-CH$_2$CH=C**H**$_2$), 4.49 (t, *J* = 5.2 Hz, 1H, C(2)-**H**), 3.95 (m, 1H, C(4)-**H**), 3.62 (m, 1H, C(6)-**H**), 2.04-2.4 (m, 4H, C(4)-C**H**$_2$,C(6)-C**H**$_2$), 1.57-1.72 (m, 3H, one of C(2)-C**H**$_2$CH$_3$, C(5)-C**H**$_2$), 1.21 (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 133.8, 117.4, 102.5, 75.4, 74.6, 40.4, 40.2, 38.4, 28.0, 8.5; IR (thin film) 3068, 2931, 2842, 2725, 1641, 1465, 1416, 1371, 1342, 1303, 1121, 969, 910, 866 cm^{-1}; HRMS (FAB+) calcd for $C_{10}H_{16}ClHgO_2$: 401.0506, found 401.0511.

***cis-cis*-4-Chloromercurymethyl-2-ethyl-6-(*E*-1-propenyl)-1,3-dioxane (entry 5, Table 1):**

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.70-5.78 (m, 1H, C(6)-C**H**=CHCH$_3$), 5.51-5.53 (m, 1H, C(6)-CH=C**H**CH$_3$), 4.54 (t, *J* = 5.1 Hz, 1H, C(2)-**H**), 4.02 (m, 2H, C(4)-**H**, C(6)-**H**), 2.31 (dd, *J* = 5 and 12 Hz, 1H, one of C(4)-C**H**$_2$), 2.07 (dd, *J* = 7 and 12 Hz, 1H, one of C(4)-C**H**$_2$), 1.56-1.72 (m, 5H, C(5)-C**H**$_2$, C(6)-CH=CHC**H**$_3$), 1.31 (m, 2H, C(2)-C**H**$_2$CH$_3$), 0.88 (t, *J* = 7.0 Hz, 3H, C(2)-CH$_2$C**H**$_3$); ^{13}C NMR (300 MHz, $CDCl_3$) δ 130.6, 128.0, 102.3, 76.5, 74.5, 40.9, 38.4, 28.1, 17.8, 8.5; IR (thin film) 2926, 2854, 1675, 1457, 1405, 1368, 1332, 1306, 1270, 1249, 1218, 1135, 1026, 969, 927, 912, 865, 798, 735, 668 cm^{-1}; HRMS (FAB+) calcd for $C_{10}H_{17}ClHgO_2$: 441.0213, found 441.0222.

***cis-cis*-4-Chloromercurymethyl-5,5-dimethyl-2-ethyl-6-pentyl-1,3-dioxane (entry 6, Table 1):**

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.52 (t, *J* = 5.2 Hz, 1H, C(2)-**H**), 3.55 (m, 1H, C(4)-**H**), 3.10 (m, 1H, C(6)-**H**), 2.16 (m, 2H, C(4)-C**H**$_2$), 1.27-1.64 (m, 10H, C(2)-C**H**$_2$CH$_3$, (C**H**$_2$)$_4$), 0.93 (m, 9H, C(2)-CH$_2$C**H**$_3$, (CH$_2$)$_4$C**H**$_3$, C(5)-C**H**$_3$), 0.75 (s, 3H, C(5)-C**H**$_3$); ^{13}C NMR (300 MHz, $CDCl_3$) δ 103.3, 85.8, 83.4, 37.4, 32.6, 31.8, 28.8, 28.0, 26.4, 22.6, 21.2, 14.1, 13.0, 8.5; IR (thin film) 2950, 2862, 1465, 1411, 1386, 1342, 1308, 1136, 1097, 1053, 939, 925, 797, 670 cm^{-1}; HRMS (FAB+) calcd for (M-1) $C_{14}H_{26}ClHgO_2$: 459.1280, found 459.1289.

Stereochemical Proofs. Selective 1D NOESY spectra were recorded for every compound reported here. In every case the illustrated enhancements were observed, establishing the all-*cis* stereochemistry.