Supporting Information

Disiloxane-protected 2-deoxyribonolactone as an efficient precursor to 1,2-dideoxy-1-β-aryl-D-ribofuranoses

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General Experimental: All solvents and reagents were purchased from commercial sources. THF was dried over and distilled from sodium/benzophenone ketyl immediately prior to use. DMF was dried over and distilled at reduced pressure from CaH_2. All other materials were used as received from the vendor. ^1H NMR spectra were recorded at 360 MHz and ^{13}C NMR spectra were recorded at 90 MHz using a Brüker AM-360 spectrometer. Chemical shifts are reported in ppm from an internal reference, tetramethylsilane. Ratios of anomers (β:α) were determined by integration of resolved peaks in the ^1H NMR spectrum of the mixed material. Assignments of the anomeric stereochemistry for compounds **3a-g** were confirmed by NOE experiments. High resolution mass spectra were recorded using a VG Autospec Mass Spectrometer operating in EI mode (70 eV).

3,5-*O*-((1,1,3,3-tetraisopropyl)disiloxanediyl)-2-deoxy-D-ribono-1,4-lactone (2b)

To a solution of 2-deoxy-D-ribose (1.00 g, 7.45 mmol) in water (6 mL) was added Br_2 (2 mL). The flask was sealed, and the contents were stirred at room temperature for 5 d. The resulting mixture was neutralized by adding Ag_2CO_3 until the pH of solution was 7.0. The mixture was filtered, and the filtrate was concentrated under reduced pressure at 40 °C to yield 2-deoxyribonolactone as a yellow oil.

Without further purification, the crude oil was dissolved in 20 mL of anhydrous DMF, and imidazole (1.27 g, 18.6 mmol) and 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (5.84 mL,

11.2 mmol) were added. The resulting solution was stirred at the room temperature for 24 h, and extracted with ether. The organic layer was washed with water, saturated aqueous $NaHCO_3$, and brine, was dried over anhydrous Na_2SO_4, and was concentrated *in vacuo*. Flash chromatography of the crude product (silica gel, CH_2Cl_2) produced the desired product as a colorless oil (2.42 g, 86%).

^{1}H NMR ($CDCl_3$) δ 4.67-4.59 (m, 1H, H-3), 4.21 (app dt, 1H, *J* = 3.6, 6.7 Hz, H-4), 4.14 (dd, 1H *J* = 12.3, 3.6 Hz, H-5), 3.92 (dd, 1H, *J* = 12.3, 6.7 Hz, H-5), 2.85 (dd, 1H, *J* = 17.3, 8.0 Hz, H-2), 2.70 (dd, 1H, *J* = 17.3, 9.2 Hz, H-2), 1.13-1.00 (m, 28H, 4 × -$CH(CH_3)_2$). ^{13}C NMR ($CDCl_3$) δ 173.0, 84.8, 69.7, 62.3, 37.8, 17.4, 17.3, 17.1, 17.0, 16.85, 16.8, 13.3, 13.1, 12.8, 12.5.

General Procedure for Synthesis of 3,5-O-((1,1,3,3-tetraisopropyl)disiloxanediyl)-1,2-dideoxy-β-1-aryl-D-ribofuranoses (3a-g)

To a solution of the bromoarene (~1 mmol) in anhydrous THF (2.5 mL) under N_2 and at –78 °C was added *n*-BuLi (~1.8 M in hexanes, 1.0 eq). The mixture was stirred at –78 °C for 30 min and was then added via cannula to a solution of **2b** (0.22 g, 0.64 mmol) in anhydrous THF (2.5 mL) at –78 °C. After 1 h, the reaction mixture was quenched at –78 °C with sat. aqueous NH_4Cl and was then extracted with diethyl ether. The combined ether phases were washed with sat. aqueous NH_4Cl, water, and brine, and were dried over anhydrous Na_2SO_4. Concentration *in vacuo* produced an oil that was used without further purification.

A solution of the crude oil in CH_2Cl_2 (2.5 mL) under N_2 and at -78 °C was treated with Et_3SiH (3 equiv.) and BF_3•OEt_2 (3 equiv.). The resulting solution was stirred at –78 °C for 6 h, and then the reaction was quenched at –78 °C by the addition of sat $NaHCO_3$. The resulting mixture was extracted with diethyl ether. The combined organic phases were washed with sat. $NaHCO_3$, water, and brine. This solution was dried over anhydrous Na_2SO_4 and was concentrated *in vacuo*. Flash chromatography of the crude product (silica gel, toluene) yielded the desired compound as an oil.

3,5-O-((1,1,3,3-tetraisopropyl)disiloxanediyl)-1,2-dideoxy-β-1-phenyl-D-ribofuranose (3a, total yield 56%, 11:1 β/α)

^{1}H NMR ($CDCl_3$) δ 7.34-7.30 (m, 5H), 5.09 (app t, 1H, *J* = 7.3 Hz, H-1), 4.55-4.51 (m, 1H, H-3), 4.14 (br d, 1H, *J* = 8.3 Hz, H-5), 3.93-3.85 (m, 2H, H-4/H-5), 2.37 (ddd, 1H, *J* = 12.8, 7.0, 4.5 Hz, H-2$_\alpha$), 2.08 (app dt, 1H, *J* = 12.8, 7.8 Hz, H-2$_\beta$), 1.09-1.02 (m, 28H, 4 × -CH(CH_3)$_2$). ^{13}C NMR ($CDCl_3$) δ 142.0, 128.3, 127.5, 125.8, 86.4, 79.1, 73.4, 63.8, 43.2,17.6, 17.4, 17.3, 17.1, 17.0, 13.5, 13.4, 13.0, 12.6. HRMS: Calcd for $C_{20}H_{33}O_4Si_2$ ([M-isopropyl]$^+$) *m/z* 393.1917, found *m/z* 393.1932.

3,5-O-((1,1,3,3-tetraisopropyl)disiloxanediyl)-1,2-dideoxy-β-1-(4-methylphenyl)-D-ribofuranose (3b, total yield 24%, 28:1 β/α)

^{1}H NMR ($CDCl_3$) δ 7.23 (d, 2H, *J* = 8.0 Hz), 7.13 (d, 2H, *J* = 8.0 Hz), 5.05 (app t, 1H, *J* = 7.4 Hz, H-1), 4.55-4.50 (m, 1H, H-3), 4.13 (dd, 1H *J* = 10.3, 2.4 Hz, H-5), 3.93-3.83 (m, 2H, H-4/H-5), 2.37-2.27 (m, 1H, H-2$_\alpha$), 2.31 (s, 3H, CH_3), 2.06 (app dt, 1H, *J* = 12.9, 7.9, H-2$_\beta$), 1.09-1.02 (m, 28H, 4 × -CH(CH_3)$_2$). ^{13}C NMR ($CDCl_3$) δ 139.0, 137.1, 129.0, 125.8, 86.4, 79.0, 73.6, 63.89, 43.2, 21.1, 17.6, 17.45, 17.4, 17.3, 17.12, 17.1, 17.0, 13.5, 13.4, 13.0, 12.6. HRMS: Calcd for $C_{21}H_{35}O_4Si_2$ ([M-isopropyl]$^+$) *m/z* 407.2073, found *m/z* 407.2056.

3,5-O-((1,1,3,3-tetraisopropyl)disiloxanediyl)-1,2-dideoxy-β-1-(3-methylphenyl)-D-ribofuranose (3c, total yield 35%, 15:1 β/α)

^{1}H NMR ($CDCl_3$) δ 7.21 (t, 1H, *J* = 7.5 Hz), 7.15 (s, 1H), 7.12 (d, 1H, *J* = 7.5 Hz), 7.06 (d, 1H, *J* = 7.3 Hz), 5.05 (app t, 1H, *J* = 7.4 Hz, H-1), 4.55-4.51 (m, 1H, H-3), 4.17-4.11 (m, 1H, H-5), 3.92-3.85 (m, 2H, H-4/H-5), 2.38-2.31 (m, 1H, H-2$_\alpha$), 2.33 (s, 3H, CH_3), 2.08 (app dt, 1H, *J* = 12.8, 7.9 Hz, H-2$_\beta$), 1.10-1.01 (m, 28H, 4 × -CH(CH_3)$_2$). ^{13}C NMR ($CDCl_3$) δ 141.9, 138.0, 128.2, 126.5, 123.0, 86.4, 79.1, 73.4, 63.8, 43.1, 21.4, 17.6, 17.5, 17.42, 17.4, 17.2, 17.1, 17.07, 17.0, 13.5, 13.4, 13.0, 12.6. HRMS: Calcd for $C_{21}H_{35}O_4Si_2$ ([M-isopropyl]$^+$) *m/z* 407.2073, found *m/z* 407.2086.

3,5-O-((1,1,3,3-tetraisopropyl)disiloxanediyl)-1,2-dideoxy-β-1-(2-methylphenyl)-D-ribofuranose (3d, total yield 17%, 6.5:1 β/α)

^{1}H NMR ($CDCl_3$) δ 7.51-7.49 (m, 1H), 7.21-7.10 (m, 3H), 5.25 (app t, 1H, *J* = 7.3 Hz, H-1), 4.53-4.48 (m, 1H, H-3), 4.15 (dd, 1H, *J* = 11.8, 3.4 Hz, H-5), 3.95 (dd, 1H, *J* = 11.8, 6.6 Hz, H-5), 3.99-3.84 (m, 1H, H-4), 2.40 (ddd, 1H, *J* = 12.6, 7.5, 5.3 Hz, H-2$_\alpha$), 2.30 (s, 3H, CH_3), 1.99 (app dt, 1H, *J* = 12.6, 7.5 Hz, H-2$_\beta$), 1.13-0.92 (m, 28H, 4 × -$CH(CH_3)_2$). ^{13}C NMR ($CDCl_3$) δ 140.7, 134.2, 130.0, 127.0, 126.1, 124.7, 85.6, 75.9, 72.6, 63.2, 41.6, 19.1, 17.6, 17.4, 17.37, 17.2, 17.1, 17.0, 13.5, 13.3, 13.0, 12.6. HRMS: Calcd for $C_{21}H_{35}O_4Si_2$ ([M-isopropyl]$^+$) *m/z* 407.2073, found *m/z* 407.2098.

3,5-*O*-((1,1,3,3-tetraisopropyl)disiloxanediyl)-1,2-dideoxy-β-1-(3,5-dimethylphenyl)-D-ribofuranose (3e, total yield 34%, 11:1 β/α)

^{1}H NMR ($CDCl_3$) δ 6.95 (s, 2H), 6.89 (s, 1H), 5.02 (app t, 1H, *J* = 7.4 Hz, H-1), 4.55-4.50 (m, 1H, H-3), 4.17-4.11 (m, 1H, H-5), 3.92-3.86 (m, 2H, H-4/H-5), 2.37-2.30 (m, 1H, H-2$_\alpha$), 2.30 (s, 6H, CH_3), 2.08 (app dt, 1H, J = 12.8, 7.9 Hz, H-2$_\beta$) 1.12-0.93 (m, 28H, 4 × -$CH(CH_3)_2$). ^{13}C NMR ($CDCl_3$) δ 141.9, 137.9, 129.1, 123.6, 86.4, 79.2, 73.4, 63.7, 43.0, 21.3, 17.6, 17.5, 17.4, 17.3, 17.1, 17.09, 17.0, 13.5, 13.4, 13.0, 12.6. HRMS: Calcd for $C_{22}H_{37}O_4Si_2$ ([M-isopropyl]$^+$) *m/z* 421.2230, found *m/z* 421.2241.

3,5-*O*-((1,1,3,3-tetraisopropyl)disiloxanediyl)-1,2-dideoxy-β-1-(2-naphthyl)-D-ribofuranose (3f, total yield 38%, 10:1 β/α)

^{1}H NMR ($CDCl_3$) δ 7.83-7.81 (m, 4H), 7.48-7.43 (m, 3H), 5.28 (app t, 1H, *J* = 7.3 Hz, H-1), 4.62-4.57 (m, 1H, H-3), 4.23-4.17 (m, 1H, H-5), 4.00-3.93 (m, 2H, H-4/H-5), 2.49-2.42 (m, 1H, H-2$_\alpha$), 2.17 (app dt, 1H, J = 12.8, 7.7 Hz, H-2$_\beta$) 1.12–1.02 (m, 28H, 4 × -$CH(CH_3)_2$). ^{13}C NMR ($CDCl_3$) δ 139.6, 133.3, 132.9, 128.2, 127.9, 127.6, 126.0, 125.7, 124.4, 124.0, 86.4, 79.1, 73.2, 63.6, 43.1, 17.6, 17.5, 17.45, 17.4, 17.2, 17.1, 17.0, 1 13.5, 13.4, 13.0, 12.6. HRMS: Calcd for $C_{24}H_{35}O_4Si_2$ ([M-isopropyl]$^+$) *m/z* 443.2073, found *m/z* 443.2094.

3,5-*O*-((1,1,3,3-tetraisopropyl)disiloxanediyl)-1,2-dideoxy-β-1-(1-naphthyl)-D-ribofuranose (3g, total yield 34%, 11:1 β/α)

^{1}H NMR ($CDCl_3$) δ 7.93 (br d, 1H, *J* = 7.8 Hz), 7.88-7.86 (m, 1H), 7.77-7.75 (m, 2H), 7.54-7.43 (m, 3H), 5.82 (app t, 1H, *J* = 7.1 Hz, H-1), 4.55 (m, 1H, H-3), 4.21 (dd, 1H,, *J* = 12.0, 3.5 Hz H-5), 4.06 (dd, 1H, *J* = 12.0, 6.0 Hz, H-5), 4.00-3.96 (m, 1H, H-4), 2.67-2.59 (ddd, 1H, J = 12.5, 7.5, 5.9 Hz, H-2$_\alpha$), 2.23-2.16 (app dt, 1H, *J* = 12.5, 7.1 Hz, H-2$_\beta$), 1.12-0.98 (m, 28H, 4 × -$CH(CH_3)_2$). ^{13}C NMR ($CDCl_3$) δ 138.3, 133.6, 130.1, 128.8, 127.6, 125.9, 125.5, 125.4, 123.1, 122.2, 85.5, 75.8, 72.2, 62.9, 42.1, 17.6, 17.5, 17.4, 17.2, 17.1, 17.08, 17.0, 13.5, 13.4, 13.0, 12.6. HRMS: Calcd for $C_{24}H_{35}O_4Si_2$ ([M-isopropyl]$^+$) *m/z* 443.2079, found *m/z* 443.2084.

General Procedure for Removal of Disiloxane Group

To a solution of the disiloxane (~0.1 mmol) in anhydrous THF (2 mL) was added $Bu_4N^+F^-$ (1 M in THF, 3.0 eq). The resulting mixture was stirred at the room temperature for 3 h, and then 5% aqueous NH_4HCO_3 solution was added to quench the reaction. The mixture was extracted with diethyl ether, and the combined organic extracts were washed with 5% aqueous NH_4HCO_3, water, and brine. The organic portion was dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to give the crude product as white solid. The crude material was purified using flash column chromatography (silica gel, 19:1 CH_2Cl_2/MeOH).

1,2-dideoxy-β-1-phenyl-D-ribofuranose[1] (1a, 70% isolated yield)

^{1}H NMR (1:1 $CDCl_3$/CD_3OD) δ 7.39-7.24 (m, 5H), 5.15 (dd, 1H, *J* = 10.3, 5.4 Hz, H-1), 4.35-4.33 (m, 1H, H-3), 3.98 (dt, 1H, *J* = 2.5, 5.1 Hz, H-4), 3.76-3.65 (m, 2H, H-5), 2.22 (ddd, 1H, *J* = 13.1, 5.3, 1.6 Hz, H-2), 1.99 (ddd, 1H, *J* = 13.1, 10.5, 6.0 Hz, H-2). ^{13}C NMR (1:1 $CDCl_3$/CD_3OD) δ 141.0, 127.7, 127.0, 125.4, 87.2, 79.8, 72.6, 62.4, 43.0. HRMS: Calcd for $C_{11}H_{14}O_3$ *m/z* 194.0943, found *m/z* 194.0934.

1,2-dideoxy-β-1-(4-methylphenyl)-D-ribofuranose (1b, 66% isolated yield)

^{1}H NMR (1:1 $CDCl_3/CD_3OD$) δ 7.26 (d, 2H, J = 7.8 Hz), 7.15 (d, 2H, J = 7.8 Hz), 5.10 (dd, 1H, J = 10.3, 5.4 Hz, H-1), 4.35-4.33 (m, 1H, H-3), 3.98-3.95 (m, 1H, H-4), 3.74-3.64 (m, 2H, H-5), 2.33 (s, 3H, CH_3), 2.22-2.17 (m, 1H, H-2), 2.02-1.98 (m, 1H, H-2). ^{13}C NMR (1:1 $CDCl_3/CD_3OD$) δ 137.8, 136.8, 128.4, 125.5, 87.1, 79.7, 72.6, 62.4, 42.9, 20.1. HRMS: Calcd for $C_{12}H_{16}O_3$ m/z 208.1099, found m/z 208.1074.

1,2-dideoxy-β-1-(3-methylphenyl)-D-ribofuranose (1c, 74% isolated yield)

^{1}H NMR (1:1 $CDCl_3/CD_3OD$) δ 7.24-7.13 (m, 3H), 7.09 (d, 1H, J = 7.2 Hz), 5.12 (dd, 1H, J = 10.4, 5.4 Hz, H-1), 4.34-4.33 (m, 1H, H-3), 3.97 (app dt, 1H, J = 2.6, 5.2 Hz, H-4), 3.72 & 3.68 (AB part of ABX, 2H, J_{AB} = 11.6 Hz, J_{AX} = 5.2 Hz, J_{BX} = 5.4 Hz, H-5), 2.34 (s, 3H, CH_3), 2.22 (ddd, 1H, J = 13.3, 5.5, 1.6 Hz, H-2), 1.99 (ddd, 1H, J = 13.3, 10.4, 6.0 Hz, H-2). ^{13}C NMR (1:1 $CDCl_3/CD_3OD$) δ 140.8, 137.4, 127.8, 127.7, 126.1, 122.5, 87.1, 79.8, 72.6, 62.4, 42.9, 20.4. HRMS: Calcd for $C_{12}H_{16}O_3$ m/z 208.1099, found m/z 208.1073.

1,2-dideoxy-β-1-(2-methylphenyl)-D-ribofuranose (1d, 67% isolated yield)

^{1}H NMR (1:1 $CDCl_3/CD_3OD$) δ 7.51 (d,1H, J = 6.9 Hz), 7.21-7.11 (m, 3H), 5.37 (dd, 1H, J = 10.2, 5.4 Hz, H-1), 4.35-4.33 (m, 1H, H-3), 3.99-3.95 (m, 1H, H-4), 3.76 & 3.71 (AB part of ABX, 2H, J_{AB} = 11.6 Hz, J_{AX} = 5.3 Hz, J_{BX} = 5.4 Hz, H-5), 2.30 (s, 3H, CH_3), 2.28 (ddd, 1H, J = 13.2, 5.4, 1.8 Hz, H-2), 1.88 (ddd, 1H, J = 13.2, 10.3, 6.2 Hz, H-2). ^{13}C NMR (1:1 $CDCl_3/CD_3OD$) δ 139.2, 134.1, 129.5, 126.6, 125.5,124.2, 86.7, 76.4, 72.6, 62.4, 41.5, 18.1. HRMS: Calcd for $C_{12}H_{16}O_3$ m/z 208.1099, found m/z 208.1104.

1,2-dideoxy-β-1-(3,5-dimethylphenyl)-D-ribofuranose (1e, 69% isolated yield)

^{1}H NMR (1:1 $CDCl_3/CD_3OD$) δ 6.98 (s, 2H), 6.91 (s, 1H), 5.08 (dd, 1H, H-1, J = 10.4, 5.4 Hz), 4.34-4.32 (m, 1H, H-3), 3.96 (app dt, 1H, J = 2.7, 5.3 Hz, H-4), 3.72 & 3.67 (AB part of ABX, 2H, J_{AB} = 11.6 Hz, J_{AX} = 5.2 Hz, J_{BX} = 5.4 Hz, H-5), 2.30 (s, 6H, 2 × CH_3), 2.18 (ddd, 1H, J =

13.2, 5.4, 1.6 Hz, H-2), 1.98 (ddd, 1H, *J* = 13.2, 10.5, 6.0 Hz, H-2). ^{13}C NMR (1:1 $CDCl_3/CD_3OD$) δ 140.8, 137.3, 128.7, 123.3, 87.1, 79.8, 72.6, 62.5, 42.9, 20.3. HRMS: Calcd for $C_{13}H_{18}O_3$ *m/z* 222.1256, found *m/z* 222.1234.

1,2-dideoxy-β-1-(2-naphthyl)-D-ribofuranose (1f, 76% isolated yield)[2]

^{1}H NMR (1:1 $CDCl_3/CD_3OD$) δ 7.84-7.82 (m, 4H), 7.51-7.45 (m, 3H), 5.32 (dd, 1H, *J* = 10.2, 5.4 Hz, H-1), 4.40-4.38 (m, 1H, H-3), 4.04-3.98 (m, 1H, H-4), 3.77-3.72 (m, 2H, H-5), 2.31 (br dd, 1H, *J* = 13.0, 5.2 Hz, H-2), 2.09 (ddd, 1H, *J* = 13.0, 10.5, 6.0 Hz, H-2). ^{13}C NMR (1:1 $CDCl_3/CD_3OD$) δ 138.5, 132.8, 132.6, 127.6, 127.3, 127.0, 125.5, 125.2, 124.2, 123.5, 87.3, 79.9, 72.67, 62.5, 43.0. HRMS: Calcd for $C_{15}H_{16}O_3$ *m/z* 244.1099, found *m/z* 244.1103.

1,2-dideoxy-β-1-(1-naphthyl)-D-ribofuranose (1g, 69% isolated yield)[2]

^{1}H NMR (1:1 $CDCl_3/CD_3OD$) δ 8.06 (d, 1H, *J* = 7.6 Hz), 7.88-7.85 (m, 1H), 7.78 (d, 1H, *J* = 8.2 Hz), 7.74 (d, 1H, *J* = 7.0 Hz) 7.56-7.44 (m, 3H), 5.91 (dd, 1H, *J* = 10.1, 5.6 Hz, H-1), 4.40-4.37 (m, 1H, H-3), 4.11-4.07 (m, 1H, H-4), 3.81 & 3.76 (AB part of ABX, 2H, J_{AB} = 11.6 Hz, J_{AX}= 5.3 Hz, J_{BX}= 5.1 Hz, H-5), 2.51 (ddd, 1H, *J* = 13.2, 5.6, 2.0 Hz, H-2), 2.05 (ddd, 1H, *J* = 13.2, 10.2, 6.2 Hz, H-2). ^{13}C NMR (1:1 $CDCl_3/CD_3OD$) δ 137.0, 133.2, 130.1, 128.1, 127.2, 125.4, 124.9, 122.5, 121.4, 86.8, 76.5, 72.5, 62.4, 42.1. HRMS: Calcd for $C_{15}H_{16}O_3$ *m/z* 244.1099, found *m/z* 244.1085.

References

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