SUPPORTING INFORMATION

A Set of Nonpolar Thymidine Nucleoside Analogues with Gradually Increasing Size

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General Synthesis Procedures

General Procedure for Synthesis of 3',5'-O-((1,1,3,3-tetraisopropyl)disiloxanediyl)-1',2'-dideoxy- β -1-aryl-D-ribofuranoses (**1b**, **3b**, **4b**)¹

To a solution of the bromoarene or iodoarene (~4.2 mmol) in anhydrous THF (5 mL) under Ar and at -78°C was added *n*-BuLi (~1.6 M in hexanes, 1.0 equiv.) and the mixture was stirred at -78°C for 30 min. To the solution was added via cannula a solution of the disiloxane-protected deoxyribonolactone **7** (1.0 g, 2.7 mmol) in anhydrous THF (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 (5 mL) under Ar and at -78°C was treated with Et_3SiH (3 equiv.) and $\text{BF}_3\cdot\text{OEt}_2$ (3 equiv.). The resulting solution was stirred at -78°C for 3 h, and then the reaction was quenched at -78°C by the addition of satd. 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*.

General Procedure for Removal of Disiloxane Group

To a solution of the disiloxane (**nb**, ~0.5 mmol) in anhydrous THF (10 mL) was added $\text{Bu}_4\text{N}^+\text{F}^-$ (1 M in THF, 3.0 equiv.). The resulting mixture was stirred at the room temperature for 2 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. The crude material was purified using column chromatography (silica gel, 40 : 1 to 20 : 1 $\text{CH}_2\text{Cl}_2/\text{MeOH}$).

Nucleoside Synthesis and Characterization

3',5'-O-((1,1,3,3-Tetraisopropyl)disiloxanediyl)-2'-deoxy-D-ribo-1',4'-lactone (7)

To a solution of 2-deoxy-D-ribose (4.50 g, 33.5 mmol) in water (30 mL) was slowly added Br₂ (9 mL). The flask was sealed, and the contents were stirred at room temperature for 5 d. The resulting mixture was neutralized by adding Ag₂CO₃ until the pH of solution was 7.0. The mixture was filtered through Celite[®] 545 and the filtrate was re-filtered after adding some amount of Celite[®] 545 to remove a fine precipitate. The filtrate was concentrated under reduced pressure to yield 2-deoxyribonolactone as yellow oil.

Without further purification, the crude oil was dissolved in anhydrous DMF (60 mL) and imidazole (5.72 g, 84.0 mmol) was added. To the solution was slowly added 1,3-dichloro-1,1,3,3-tetraisopropylidisiloxane (15 g, 47.6 mmol) via dropping funnel during 1 hour. 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 NaHCO₃, and brine, was dried over anhydrous Na₂SO₄, and was concentrated *in vacuo*. Flash chromatography of the crude product (silica gel, CH₂Cl₂) produced the desired product as a colorless oil (9.00 g, 24.0 mmol, 72 %).

¹H NMR (CDCl₃, ppm) 4.66-4.61 (m, 1H, H-3'), 4.23-4.20 (m, 1H, H-4'), 4.14 (dd, 1H, J = 13.5, 3.5 Hz, H-5'), 3.94 (dd, 1H, J = 12.5, 6.5 Hz, H-5') 2.86 (dd, 1H, J = 17.0, 8.0 Hz, H-2'), 2.87 (dd, 1H, J = 17.5, 9.5 Hz, H-2'), 1.10-1.00 (m, 28H, 4 x -CH(CH₃)₂);

¹³C NMR (CDCl₃, ppm) 173.2 (carbonyl), 85.0, 69.8, 62.5, 38.0, 17.6, 17.5, 17.4, 17.2, 17.1, 17.0, 13.5, 13.3, 13.0, 12.7;

HRMS (DCI+, NH₃) calcd mass 392.2288 for [C₁₇H₃₄O₅Si₂+NH₄], found 392.2275 for [M+NH₄]⁺.

Dihydrogen Analogue:

3',5'-O-((1,1,3,3-Tetraisopropyl)disiloxanediyl)-1',2'-dideoxy-β-1'-(3-methylphenyl)-D-ribofuranose (1b)

Scale: 3-Bromotoluene (0.71 g, 4.2 mmol), **7** (1.0 g, 2.7 mmol), *n*-BuLi (1.6 M in hexane, 2.6 mL).

Column conditions: Flash chromatography of the crude product (silica gel, toluene) yielded the desired compound ($\approx 5 : 1$ β/α mixture, 0.43 g) as an oil. The following flash chromatography of the β/α mixture (silica gel, 1 : 1 $\text{CH}_2\text{Cl}_2/\text{toluene}$) yielded the desired isomer ($\approx 30 : 1$ β/α mixture, 0.37 g, 0.82 mmol, 30%) as an oil.

^1H NMR (CDCl_3 , ppm) 7.21 (app t, 1H, $J = 7.5$ Hz), 7.15-7.11 (m, 2H), 7.07 (d, 1H, $J = 7.5$ Hz), 5.05 (app t, 1H, $J = 7.5$ Hz, H-1'), 4.53-4.51 (m, 1H, H-3'), 4.14-4.11 (m, 1H, H-5'), 3.91-3.86 (m, 2H, H-4' + H-5'), 2.37-2.32 (m, 4H, CH_3 + H-2' $_{\alpha}$), 2.10-2.04 (m, 1H, H-2' $_{\beta}$), 1.12-0.94 (m, 28H, 4 x $-\text{CH}(\text{CH}_3)_2$);

^{13}C NMR (CDCl_3 , ppm) 142.1, 138.2, 128.5, 126.7, 123.2, 86.6, 79.3, 73.5, 63.9, 43.3, 21.7, 17.8, 17.7, 17.6, 17.5, 17.3, 17.2, 13.7, 13.2, 12.8;

HRMS (DCI^+ , NH_3) calcd mass 468.2965 for $[\text{C}_{24}\text{H}_{42}\text{O}_4\text{Si}_2+\text{NH}_4]^+$, found 468.2977 for $[\text{M}+\text{NH}_4]^+$.

1',2'-Dideoxy- β -1'-(3-methylphenyl)-D-ribofuranose (1)

^1H NMR (CDCl_3 , ppm) 7.12 (app t, 1H, $J = 7.5$ Hz), 7.02-6.99 (m, 3H), 5.01 (dd, 1H, $J = 10.5$, 5.5 Hz, H-1'), 4.22 (br, 1H, H-3'), 3.90-3.87 (m, 1H, H-4'), 3.59 (br, 2H, H-4' + H-5'), 2.24 (s, 3H, CH_3), 2.09 (ddd, 1H, $J = 13.5$, 5.5, 1.5 Hz, H-2'), 1.89-1.83 (m, 1H, H-2'');

^{13}C NMR (CDCl_3 , ppm) 141.1, 138.4, 128.8, 128.6, 127.0, 123.3, 87.5, 80.5, 73.7, 63.5, 43.5, 21.7;

HRMS (DEI^+) calcd mass 208.1096 for $[\text{C}_{12}\text{H}_{16}\text{O}_3]$, found 208.1105 $[\text{M}]^+$;

UV-visible (MeOH) $\epsilon = 250 \text{ M}^{-1}\text{cm}^{-1}$ at $\lambda = 260 \text{ nm}$, $\epsilon = 210 \text{ M}^{-1}\text{cm}^{-1}$ at $\lambda = 270 \text{ nm}$.

Difluoro Analogue:

(Note that although this nucleoside analogue was reported previously², this is a new procedure.)

5-Bromo-2,4-difluorotoluene (2a)

^1H NMR (CDCl_3 , ppm) 7.36 (app t, 1H, $J = 7.0$ Hz, Ar-H6), 6.84 (app t, 1H, $J = 9.0$ Hz, Ar-H3), 2.22 (s, 3H, CH_3);

^{13}C NMR (CDCl_3 , ppm) 160.3 (dd, $^1J_{\text{CF}} = 247$, $^3J_{\text{CF}} = 10.5$ Hz), 157.5 (dd, $^1J_{\text{CF}} = 246$, $^3J_{\text{CF}} = 11.9$ Hz), 134.9, 122.6 (d, $^2J_{\text{CF}} = 22.4$ Hz), 104.5 (app t, $^2J_{\text{CF}} = 27.1$ Hz), 103.2 (d, $^2J_{\text{CF}} = 20.5$ Hz), 14.0;

HRMS (GCMS +) calcd mass 205.9542 for $[C_7H_5BrF_2]$, found 205.9552 for $[M]^+$.

3',5'-O-((1,1,3,3-Tetraisopropyl)disiloxanediyl)-1',2'-dideoxy- β -1'-(2,4-difluoro-5-methylphenyl)-D-ribofuranose (2b)

Dry THF (5.0 mL) was placed in a round-bottomed flask equipped with a condenser, drying tube and additional funnel. Magnesium turnings (0.24 g, 9.9 mmol) and a few crystals of iodine were added. **2a** (2.1 g, 10 mmol) was added dropwise to the mixture. Slight heating was needed (40°C) to drive the reaction to completion. After formation of the Grignard reagent was complete (~1 h), **7** (2.1 g, 5.6 mmol) dissolved in THF was added dropwise via an additional funnel over a period of 1 hour. The solution was stirred at room temperature for 2 hours. The reaction mixture was quenched with sat'd aqueous NH_4Cl and was then extracted with diethyl ether. The combined ether phases were washed with sat'd 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.

For the reduction, the typical Woski's method (Et_3SiH , $BF_3 \cdot OEt_2$) was followed.

Column condition: Flash chromatography of the crude product (silica gel, toluene) yielded the desired compound (5 : 1 β/α mixture) as an oil. The following flash chromatography of the β/α mixture (silica gel, 1 : 1 : 1 hexanes/ CH_2Cl_2 /toluene) yielded the desired isomer (102 mg, total yield 9.8%) as an oil.

1H NMR ($CDCl_3$, ppm) 7.28 (app t, 1H, $J_{HF} = 8.4$ Hz, Ar-H6), 6.71 (app t, 1H, $J_{HF} = 9.6$ Hz, Ar-H3), 5.26 (app t, 1H, $J = 7.2$ Hz, H-1'), 4.51-4.46 (m, 1H, H-3'), 4.12 (app dd, 1H, $J = 12.0, 3.2$ Hz, H-5'), 3.97-3.92 (m, 1H, H-5'), 3.85-3.81 (m, 1H, H-4'), 2.44-2.38 (m, 1H, H-2' $_{\alpha}$), 2.20 (s, 3H, CH_3), 2.07-2.00 (m, 1H, H-2' $_{\beta}$), 1.12-0.93 (m, 28H, 4 x $-CH(CH_3)_2$);

^{13}C NMR ($CDCl_3$, ppm) 160.4 (d, $^1J_{CF} = 245$ Hz) 157.9 (d, $^1J_{CF} = 233$ Hz) 129.2, 125.3, 120.7, 103.2 (app t, $^2J_{CF} \approx 25$ Hz), 85.8, 72.8, 72.3, 63.0, 41.8, 17.7, 17.6, 17.45, 17.3, 17.2, 17.1, 14.2, 14.1, 13.7, 13.5, 13.1, 12.7;

HRMS (DCI+, NH_3) calcd mass 504.2776 for $[C_{24}H_{40}F_2O_4Si_2 + NH_4]^+$, found 504.2788 for $[M + NH_4]^+$.

1',2'-Dideoxy- β -1'-(2,4-difluoro-5-methylphenyl)-D-ribofuranose (2)

^1H NMR (CDCl_3 , ppm) 7.25 (app t, 1H, $J_{\text{HF}} = 8.4$), 6.74 (app t, 1H, $J_{\text{HF}} = 10.0$), 5.30 (dd, 1H, $J = 10.4, 5.6$), 4.47 (br, 1H), 4.02-3.99 (m, 1H), 3.86-3.71 (m, 2H), 2.31-2.26 (m, 1H), 2.23 (s, 3H), 2.08-1.94 (m, 1H);

^{13}C NMR (CDCl_3 , ppm) 160.8 (dd, $^1J_{\text{CF}} = 215$, $^3J_{\text{CF}} = 11$ Hz), 158.3 (dd, $^1J_{\text{CF}} = 214$, $^3J_{\text{CF}} = 11$ Hz), 129.5 (app t, $^3J_{\text{CF}} = 6$ Hz), 123.7 (dd, $^2J_{\text{CF}} = 13$, $^4J_{\text{CF}} = 4$ Hz), 120.8 (dd, $^2J_{\text{CF}} = 17$, $^3J_{\text{CF}} = 4$ Hz), 103.6 (app t, $^2J_{\text{CF}} = 26$ Hz), 87.2, 74.7, 73.7, 63.4, 42.5, 14.2;

HRMS (DCI+, NH_3) calcd mass 262.1254 for $[\text{C}_{12}\text{H}_{14}\text{F}_2\text{O}_3]$, found 262.1250 for $[\text{M}+\text{NH}_4]^+$;

UV-visible (MeOH) $\epsilon = 1000 \text{ M}^{-1}\text{cm}^{-1}$ at $\lambda = 260 \text{ nm}$, $\epsilon = 1200 \text{ M}^{-1}\text{cm}^{-1}$ at $\lambda = 270 \text{ nm}$.

Dichloro analogue:**5-Bromo-2,4-dichlorotoluene (3a)³**

2,4-Dichlorotoluene (6.4 g, 40 mmol) was placed in a two-necked round bottomed flask equipped with an addition funnel and a condenser, with a drying tube with potassium hydroxide. Iron filings (100 mg) were added and the solution was heated to 60°C . Bromine (2.1 mL, 41 mmol) was placed in the addition funnel and added to the 60°C solution dropwise over a period of two hours. Acetic acid (50 mL) was added and the solution was cooled to 30°C . The reaction was allowed to stir in the dark for 2 hours at 30°C . The solution was poured into vigorously stirred 10% aqueous sodium hydroxide. Benzene (150 mL) was added and the organic layer was washed with water, saturated NaHCO_3 and brine. The organic layer was dried over anhydrous Na_2SO_4 . The solution was filtered, concentrated and re-crystallized in methanol. The product was obtained as a white solid in 43% yield (4.0 g, 17 mmol).

^1H NMR (CDCl_3 , ppm) 7.48 (s, 1H, Ar-H6), 7.44 (s, 1H, Ar-H3), 2.33 (s, 3H, CH_3);

^{13}C NMR (CDCl_3 , ppm) 135.7, 134.4, 133.2, 131.6, 129.5, 119.5, 18.7;

HRMS (EI+) calcd mass 237.8951 for $[\text{C}_7\text{H}_5\text{BrCl}_2]$, found 237.8942 for $[\text{M}]^+$.

3',5'-O-((1,1,3,3-Tetraisopropyl)disiloxanediyl)-1',2'-dideoxy- β -1'-(2,4-dichloro-5-methylphenyl)-D-ribofuranose (3b)

Scale: **3a** (1.0 g, 4.2 mmol), **7** (1.0 g, 2.7 mmol), *n*-BuLi (1.6 M in hexane, 2.6 mL).

Column condition: Flash chromatography of the crude product (silica gel, toluene) yielded the desired compound ($\approx 5 : 1$ β/α mixture) as an oil. The following flash chromatography of the β/α mixture (silica gel, 2 : 1 to 1 : 1 hexanes/toluene) yielded the desired β isomer (0.50 g, 0.96 mmol, 35%) as an oil.

^1H NMR (CDCl_3 , ppm) 7.47 (s, 1H), 7.32 (s, 1H), 5.31 (dd, 1H, $J = 8.0, 6.0$ Hz, H-1'), 4.42 (app dd, 1H, $J = 14.4, 7.2$ Hz, H-3'), 4.11 (app dd, 1H, $J = 12.0, 3.2$ Hz, H-5'), 4.03 (app dd, 1H, $J = 12.4, 4.8$ Hz, H-5'), 3.82-3.79 (m, 1H, H-4'), 2.56-2.49 (m, 1H, H-2' $_{\alpha}$), 2.33 (s, 3H, CH_3), 1.99-1.92 (m, 1H, H-2' $_{\beta}$), 1.10-0.93 (m, 28H, 4 x $-\text{CH}(\text{CH}_3)_2$);

^{13}C NMR (CDCl_3 , ppm) 138.6, 134.1, 132.5, 128.4, 128.2, 127.8, 84.5, 74.2, 70.2, 61.3, 40.3, 18.9, 16.8, 16.7, 16.5, 16.4, 16.3, 12.7, 12.5, 12.1, 11.8;

HRMS (DCI^+ , NH_3) calcd mass 536.2185 for $[\text{C}_{24}\text{H}_{40}\text{Cl}_2\text{O}_4\text{Si}_2+\text{NH}_4]$, found 536.2176 for $[\text{M}+\text{NH}_4]^+$.

1',2'-Dideoxy- β -1'-(2,4-dichloro-5-methylphenyl)-D-ribofuranose (3)

^1H NMR (CD_3OD , ppm) 7.51 (s, 1H), 7.25 (s, 1H), 5.23 (dd, 1H, $J = 10.0, 5.5$ Hz, H-1'), 4.19-4.17 (m, 1H, H-3'), 3.84-3.82 (m, 1H, H-5'), 3.59 (br, 2H, H-5' + H-4'), 2.31-2.27 (m, 1H, H-2' $_{\alpha}$), 2.23 (s, 3H, CH_3), 1.64-1.58 (m, 1H, H-2' $_{\beta}$);

^{13}C NMR (CD_3OD , ppm) 138.9, 135.2, 133.1, 129.15, 128.94, 128.73, 87.7, 76.5, 72.9, 62.6, 42.2, 18.5;

HRMS (DEI^+) calcd mass 276.0317 for $[\text{C}_{12}\text{H}_{14}\text{Cl}_2\text{O}_3]$, found 276.0311 for $[\text{M}]^+$;

UV-visible (MeOH) $\epsilon = 250 \text{ M}^{-1}\text{cm}^{-1}$ at $\lambda = 260 \text{ nm}$, $\epsilon = 510 \text{ M}^{-1}\text{cm}^{-1}$ at $\lambda = 270 \text{ nm}$.

Dibromo analogue:

2,4-Dibromo-5-iodotoluene (4a)

Iron filings (200 mg) were added to 3-iodotoluene (6.5 g, 30 mmol) and the solution was warmed to 40°C . Bromine (3.0 mL, 2 equiv.) was slowly injected to the 40°C solution for 1 hour. The reaction mixture was heated to 60°C and stirred for 2 hours. During the reaction the small portion of glacial acetic acid (4 mL) was added for stirring. The solution was poured into vigorously stirred 5% aqueous sodium hydroxide. Toluene (200 mL) was added and the organic layer was washed with water and brine. The organic layer was dried over anhydrous Na_2SO_4 .

The solution was filtered, concentrated, and re-crystallized in methanol (200 mL) to obtain a white solid in 33% (3.9 g, 10 mmol).

^1H NMR (CDCl_3 , ppm) 7.75 (s, 1H, Ar-H3), 7.71 (s, 1H, Ar-H5), 2.30 (s, 3H, CH_3);

^{13}C NMR (CDCl_3 , ppm) 141.5, 139.0, 135.4, 127.4, 125.5, 99.5, 22.2;

HRMS (DEI^+) calcd mass 373.7802 for $[\text{C}_7\text{H}_5\text{Br}_2\text{I}]$, found 373.7800 for $[\text{M}]^+$.

3',5'-O-((1,1,3,3-Tetraisopropyl)disiloxanediyl)-1',2'-dideoxy- β -1'-(2,4-dibromo-5-methylphenyl)-D-ribofuranose (4b)

Scale: **4a** (1.5 g, 4.0 mmol), **7** (1.0 g, 2.7 mmol), *n*-BuLi (1.6 M in hexane, 2.6 mL)

Column condition: Flash chromatography of the crude product (silica gel, toluene) yielded the desired compound ($\approx 5 : 1$ β/α mixture) as an oil. The following flash chromatography of the β/α mixture (silica gel, 2 : 1 to 1 : 1 hexanes/toluene) yielded the desired β isomer (0.48 g, 0.79 mmol, 29%) as an oil.

^1H NMR (CDCl_3 , ppm) 7.72 (s, 1H), 7.37 (s, 1H), 5.24 (dd, 1H, $J = 8.4, 6.0$ Hz, H-1'), 4.42 (app dd, 1H, $J = 14.4, 7.2$ Hz, H-3'), 4.11 (app dd, 1H, $J = 12.4, 3.2$ Hz, H-5'), 4.03 (app dd, 1H, $J = 12.0, 4.8$ Hz, H-5'), 3.82-3.78 (m, 1H, H-4'), 2.58-2.51 (m, 1H, H-2' $_{\alpha}$), 2.34 (s, 3H, CH_3), 1.98-1.91 (m, 1H, H-2' $_{\beta}$), 1.13-0.93 (m, 28H, 4 x $-\text{CH}(\text{CH}_3)_2$);

^{13}C NMR (CDCl_3 , ppm) 141.8, 138.6, 134.3, 130.6, 124.4, 119.7, 85.4, 77.0, 71.1, 62.3, 41.3, 22.6, 17.8, 17.7, 17.6, 17.4, 17.3, 17.2, 13.6, 13.4, 13.0, 12.7;

HRMS (DCI^+ , NH_3) calcd mass 624.1175 for $[\text{C}_{24}\text{H}_{40}\text{Br}_2\text{O}_4\text{Si}_2]$, found 624.1185 for $[\text{M}+\text{NH}_4]^+$.

1',2'-Dideoxy- β -1'-(2,4-dibromo-5-methylphenyl)-D-ribofuranose (4)

^1H NMR (CD_3OD , ppm) 7.66 (s, 1H), 7.41 (s, 1H), 5.35 (dd, 1H, $J = 9.5, 6.0$ Hz, H-1'), 4.43 (br, 1H, H-3'), 4.05-4.02 (m, 1H, H-5'), 3.94-3.82 (br, 2H, H-5' + H-4'), 2.55-2.51 (m, 1H, H-2' $_{\alpha}$), 2.37 (s, 3H, CH_3), 1.87-1.69 (m, 1H, H-2' $_{\beta}$);

^{13}C NMR (CD_3OD , ppm) 140.4, 139.0, 134.5, 130.3, 124.4, 120.1, 87.1, 78.6, 73.7, 63.5, 42.9, 22.6;

HRMS (DEI^+) calcd mass 363.9306 for $[\text{C}_{12}\text{H}_{14}\text{Br}_2\text{O}_3]$, found 363.9305 for $[\text{M}]^+$;

UV-visible (MeOH) $\epsilon = 498 \text{ M}^{-1}\text{cm}^{-1}$ at $\lambda = 260 \text{ nm}$, $\epsilon = 594 \text{ M}^{-1}\text{cm}^{-1}$ at $\lambda = 270 \text{ nm}$.

Diiodo Analogue:**3',5'-O-((1,1,3,3-Tetraisopropyl)disiloxanediyl)-1',2'-dideoxy- β -1'-(2,4-diiodo-5-methylphenyl)-D-ribofuranose (5b)⁴**

Ace pressure tube was charged with CuI (73 mg, 0.38 mmol), NaI (2.3 g, 15 mmol), evacuated and backfilled with argon. The solution of **4b** (460 mg, 0.76 mmol) and *trans*-N, N'-dimethyl-1,2-cyclohexanediamine⁵ (148 μ L, 0.76 mmol) in 1-pentanol (2 mL) was added to the pressure tube. The reaction mixture was stirred at 130°C for 48 hours. The resulting suspension was allowed to reach room temperature. Saturated NaHCO₃ was added and the resulting mixture was extracted with diethyl ether. The combined organic phases were washed with saturated NaHCO₃, water, and brine. This solution was dried over anhydrous Na₂SO₄ and was concentrated *in vacuo*. Flash chromatography of the crude product (silica gel, 2 : 1 to 1 : 1 hexanes/toluene) yielded the desired compound (120 mg, 0.17 mmol, 22%) as an oil.

¹H NMR (CDCl₃, ppm) 7.87 (s, 1H), 7.64 (s, 1H), 5.09 (dd, 1H, J = 8.0, 5.5 Hz, H-1'), 4.41 (app dd, 1H, J = 14.5, 7.0 Hz, H-3'), 4.10 (app dd, 1H, J = 12.0, 3.0 Hz, H-5'), 4.04 (app dd, 1H, J = 12.0, 5.5 Hz, H-5'), 3.81-3.79 (m, 1H, H-4'), 2.56-2.52 (m, 1H, H-2' _{α}), 2.35 (s, 3H, CH₃), 1.93-1.89 (m, 1H, H-2' _{β}), 1.13-0.93 (m, 28H, 4 x -CH(CH₃)₂); ¹³C NMR (CDCl₃, ppm) 144.6, 142.6, 139.7, 136.8, 101.6, 96.1, 85.6, 80.8, 71.2, 62.3, 41.5, 27.5, 17.8, 17.6, 17.5, 17.3, 13.7, 13.5, 13.1, 12.8;

HRMS (MALDI⁺, CHCA) mass calcd mass 785.0229 for [C₃₃H₃₂I₂O₅Na], found 785.0260.

1',2'-Dideoxy- β -1'-(2,4-diiodo-5-methylphenyl)-D-ribofuranose (5)

¹H NMR (CDCl₃, ppm) 7.81 (s, 1H), 7.64 (s, 1H), 5.17 (dd, 1H, J = 9.2, 5.6 Hz, H-1'), 4.41-4.38 (m, 1H), 4.02-3.99 (m, 1H), 3.90-3.81 (m, 2H), 2.54-2.50 (m, 1H, H-2' _{α}), 2.35 (s, 3H, CH₃), 1.81-1.73 (m, 1H, H-2' _{β})

¹³C NMR (CDCl₃, ppm) 143.2, 142.9, 139.9, 136.5, 102.5, 96.3, 87.2, 82.5, 73.5, 63.5, 42.9, 27.4;

HRMS (DEI⁺) mass calcd 459.9032 for [C₁₂H₁₄I₂O₃], found 459.9039 for [M]⁺;

UV-visible (MeOH) ϵ = 3900 M⁻¹cm⁻¹ at λ = 260 nm, ϵ = 2300 M⁻¹cm⁻¹ at λ = 270 nm.

Confirmation of Anomeric Geometry⁶ α -anomer

Irradiation at:

H α : 0 enhancementH β : 2 enhancements β -anomer

Irradiation at:

H α : 1 enhancementH β : 1 enhancement1D ¹H-NMR NOE data for assignments of the anomeric stereochemistry of **nb**

Aryl substituent	NOE observed at:	Irradiation (%) at:	
		down field H2' α	up field H2' β
	H1'	5.1 ^a	1.1
	H3'	0.50 ^a	11
	H1'	12	1.1
	H3'	1.2	10
	H1'	14	1.8
	H3'	0.94	11
	H1'	11	1.3
	H3'	0.59	10
	H1'	12	1.2
	H3'	0.87	10

^a The peaks of H2' (2.37-2.32, m, 1H) and methyl (2.33, s, 3H) were superimposed, so the value of 1D-NOE estimation is not accurate. Nevertheless, the relative ratio of enhancement (H1' / H3' $\approx$ 10) is similar to the others.

Confirmation of Halogenated Arene Substitutions (3a, 4a)⁷

1D ¹H-NOE data for 2a, 3a, and 4a

Bromination Products	Irradiation (%) at :	NOE observed (%) at:
<i>CH</i> ₃ -	<i>ArH</i> ₁ (6.83 ppm)	0.8
		<i>ArH</i> ₂ (7.35 ppm)	1.45
	<i>CH</i> ₃ -	<i>ArH</i> ₁ (7.44 ppm)	0.3
		<i>ArH</i> ₂ (7.48 ppm)	2.2
	<i>ArH</i> ₁ (7.71 ppm)	<i>CH</i> ₃ -	4.6
		<i>ArH</i> ₂ (7.75 ppm)	1.4

5-Bromo-2,4-dichlorotoluene (3a)

From *HC* HMQC (*HC* correlation *via* one-bond *CH* coupling ¹*J*_{*CH*}), we can assign (C3, C6) or (C3, C5) pairs.

Expected *HC* HMBC for 5-Bromo-2,4-dichlorotoluene

	exptd for H6		exptd for H3	
	² <i>J</i> _{<i>CH</i>}	³ <i>J</i> _{<i>CH</i>}	² <i>J</i> _{<i>CH</i>}	³ <i>J</i> _{<i>CH</i>}
C1	➡➡			➡➡
C2		➡➡	➡➡	
C3				
C4		➡➡	➡➡	
C5	➡➡			➡➡
C6				

(C3, C6) ⇒ silent, silent

Expected *HC* HMBC for 6-Bromo-2,4-dichlorotoluene

	exptd for H5		exptd for H3	
	² <i>J</i> _{<i>CH</i>}	³ <i>J</i> _{<i>CH</i>}	² <i>J</i> _{<i>CH</i>}	³ <i>J</i> _{<i>CH</i>}
C1		➡➡		➡➡
C2			➡➡	
C3		➡➡		
C4	➡➡		➡➡	
C5				➡➡
C6	➡➡			

(C3, C5) ⇒ alternative, alternative

Observed *HC* HMBC ^{13}C NMR (CDCl_3 , ppm) 135.7, 134.4, 133.2, 131.6, 129.5, 119.5, 18.7;

134.4 or 129.5	obsd at 7.47 ppm ↔, ↔	obsd at 7.42 ppm ↔, ↔
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∴ 5-Bromo-2,4-dichlorotoluene (**3a**)**2,4-Dibromo-5-iodotoluene (4a)**

From *HC* HSQC (*HC* correlation *via* one-bond *CH* coupling $^1J_{CH}$), we can assign (C3, C6), (C4, C6) or (C2, C6) pairs.

Expected *HC* HMBC for 2,4-dibromo-5-iodotoluene

	exptd for H6		exptd for H3	
	$^2J_{CH}$	$^3J_{CH}$	$^2J_{CH}$	$^3J_{CH}$
C1	↔			↔
C2		↔	↔	
C3				
C4		↔	↔	
C5	↔			↔
C6				

(C3, C6) ⇒ silent, silent

Expected *HC* HMBC for 2,3-dibromo-5-iodotoluene

	exptd for H6		exptd for H4	
	$^2J_{CH}$	$^3J_{CH}$	$^2J_{CH}$	$^3J_{CH}$
C1	↔			
C2		↔		↔
C3			↔	
C4	↔	↔		
C5	↔		↔	
C6				↔

(C4, C6) ⇒ alternative, alternative

Expected *HC* HMBC for 3,4-dibromo-5-iodotoluene

	exptd for H6		exptd for H2	
	$^2J_{CH}$	$^3J_{CH}$	$^2J_{CH}$	$^3J_{CH}$
C1	↔		↔	
C2	↔	↔		
C3			↔	
C4		↔		↔
C5	↔			
C6				↔

(C2, C6) ⇒ alternative, alternative

Observed *HC* HMBC ^{13}C NMR (CDCl_3 , ppm) 141.5, 139.0, 135.4, 127.4, 125.5, 99.5, 22.2;

	obsd at 7.73 ppm	obsd at 7.69 ppm
141.5 or 135.4	↔, ↔	↔, ↔

∴ 2,4-Dibromo-5-iodotoluene (**4a**)

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