2-Deoxy-2-Iodo- and 2-Deoxy-2-Bromo-α-Glucopyranosyl Trichloroacetimidates: Highly Reactive and Stereoselective Donors For the Synthesis of 2-Deoxy-β-Glycosides

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SUPPORTING INFORMATION

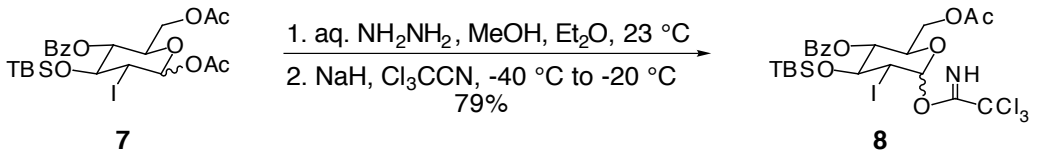
Representative experimental procedures for synthesis of the 2-deoxy-2-iodo- and 2-deoxy-2-bromo-α-glucosyl trichloroacetimidates and their glycosidation reactions; spectroscopic data for **8**-**10**, **12**, **14**, **16**, **18**, **19**, **21**-**23** and **25** (13 pages). See any current masthead page for ordering information.

General Procedures. All glycosidation reactions were conducted in flame-dried or oven-dried glassware under an atmosphere of dry nitrogen using dichloromethane distilled over P_2O_5. All solvents except dimethyl formamide, acetic anhydride, and acetic acid were purified before use. Diethyl ether and tetrahydrofuran were distilled from sodium benzophenone ketyl; triethylamine, diisopropylethylamine, dichloromethane, and pyridine were distilled from CaH_2; toluene was distilled from sodium.

^{1}H NMR spectra were measured at 300, 400, and 500 MHz on commercial NMR instruments. Chemical shifts are reported in δ with coupling constants reported in Hz. Residual chloroform (δ 7.26 ppm) was used as internal references for spectra measured in this solvent. ^{13}C NMR spectra were measured at 75, 100 or 125 MHz; chloroform (δ 77.0 ppm) was used as internal reference for spectra measured in this solvent. High resolution mass spectra were measured at 70 eV on a Kratos GC/MS 80 RFA mass spectrometer at the Indiana University Mass Spectrometry Laboratory, or on a Micromass Corp. VG 70-250-S at the University of Michigan Mass Spectrometry Laboratory. Optical rotations were measured on a Rudolph Autopol III polarimeter using a quartz cell with 1 mL capacity and a 10 cm path length. Elemental analyses were performed by Robertson Microlit Laboratories of Madison, NJ, or the University of Michigan Combustion Analysis Laboratory.

Analytical thin layer chromatography (TLC) was performed using plates coated with a 0.25 mm thickness of silica gel containing PF254 indicator (Analtech), and compounds were visualized with UV light, potassium iodide/iodine stain, *p*-anisaldehyde stain, ceric ammonium molybdate stain, or phosphomolybdic acid in EtOH. Flash chromatography was performed as described by Still[1] using Kieselgel 60 (230-400 mesh). High pressure liquid chromatography (HPLC) was performed on a system utilizing a Rainin SD-200 pump and a Rainin HPXL pump with a gradient solvent system of hexanes and ethyl acetate, a Rheodyne 7125 injector, and a Rainin UV-C UV detector at 254 nm. Depending on sample size, HPLC purifications were carried out with Rainin Dynamax-60A Si 83-111-C 10 mm, Dynamax-60A Si 83-121-C 21 mm, or Microsorb Si 80-140-C8 41 mm columns.

[1]Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923



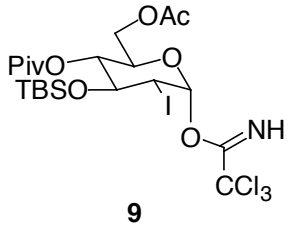
7 **8**

6-O-Acetyl-4-O-benzoyl-3-O-(*tert*-butyldimethyl)silyl-2-deoxy-2-iodo-1-trichloroacetimido-D-glucopyranose (8). To a 23 °C solution of anomeric acetates **7** (1.29 g, 2.18 mmol; 65 : 35 β : α) in MeOH (22 mL) and Et_2O (8 mL) was added 11.0 M aqueous NH_2NH_2 solution (0.40 mL, 4.4 mmol). The mixture was stirred for 0.5 h, then H_2O and EtOAc were added. The layers were separated, and the mixture was extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated. Residual MeOH and H_2O were removed by coevaporation twice with benzene and the resulting oil was dried under vacuum to afford the crude lactols (1.21 g, 99%) as a white foam. ^{1}H NMR analysis of this material revealed the desired lactols with a β : α ratio of 30 : 70 and only slightly contaminated with minor impurities. A portion of this lactol mixture (0.77 g, 1.4 mmol) was dissolved in Cl_3CCN (14 mL), and the solution was cooled to -40 °C. A 60% NaH oil dispersion (0.56 g, 14 mmol) was then added to the -40 °C solution. (Note: On larger scale, this method can result in the NaH igniting. It is therefore advisable for larger scale experiments to add a solution of the lactols in Cl_3CCN to a -40 °C mixture of 60% NaH oil dispersion in Cl_3CCN.) After being stirred for 1 h, the mixture was placed in a -20 °C freezer. After sitting in the freezer for 12 h, the mixture was filtered through Celite (pre-dried at 120-130 °C) and washed with CH_2Cl_2, never letting the Celite pad become dry and keeping the funnel under a stream of N_2. The resulting orange solution was concentrated and residual Cl_3CCN was coevaporated twice with CH_2Cl_2 to afford 1.54 g of crude material as an orange foam. The crude product was purified by flash chromatography on ca. 100 g of Davisil with 15% EtOAc/hexanes to yield 0.734 g of a yellow oil that contained the desired α-*gluco*-imidate **8** contaminated with trichloroacetamide. Based on the ^{1}H NMR spectrum and integration ratios, the mixture was determined to contain the desired α-*gluco*-imidate **8** (0.657 g, 68%) and trichloroacetamide (0.077 g). Mixed fractions containing α-*gluco*-imidate **8**, β-*gluco*-imidate **8**, and trichloroacetamide were also isolated. Based on the ^{1}H NMR spectrum and integration ratios, this mixture was determined to contain the desired α-*gluco*-imidate **8** (0.091 g, 9%),

β-*gluco*-imidate **8** (0.020 g, 2%), and trichloroacetamide (0.013 g). These chromatography fractions were used directly in subsequently described glycosidation reactions.

Data for α-*gluco*-imidate **8**: $[\alpha]_D^{26}$ +98.4° (c 2.90, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (s, 1H), 8.04-8.02 (m, 2H), 7.61-7.57 (m, 1H), 7.48-7.44 (m, 2H), 6.57 (d, *J* = 3.3 Hz, 1H), 5.34 (dd, *J* = 10.3, 8.8 Hz, 1H), 4.41 (dd, *J* = 10.3, 8.8 Hz, 1H), 4.27 (app dt, *J* = 10.3, 4.0 Hz, 1H), 4.22 (dd, *J* = 10.4, 3.1 Hz, 1H), 4.14-4.08 (m, 2H), 1.94 (s, 3H), 0.83 (s, 9H), 0.24 (s, 3H), -0.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 165.2, 160.3, 133.5, 129.9, 129.5, 128.5, 96.6, 90.9, 72.9, 71.9, 70.9, 62.4, 29.0, 26.1, 20.5, 18.1, -3.0, -3.3; IR (thin film from $CDCl_3$): 3343, 3230, 3064, 2956, 2930, 2895, 2857, 2258, 2108, 1972, 1920, 1736, 1676, 1602, 1585, 1493, 1472, 1462, 1452, 1387, 1366, 1266, 1177, 1132, 1090, 1068, 1028, 993, 968, 916, 856, 839, 796, 779, 733, 711, 688, 676, 660, 639 cm^{-1}; HRMS calcd for $C_{23}H_{31}O_7NCl_3ISiNa$ (M+Na) 715.9880, found 715.9863.

Partial data for β-*gluco*-imidate **8**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.72 (s, 1H), 8.03-8.01 (m, 2H), 7.60-7.57 (m, 1H), 7.47-7.44 (m, 2H), 6.14 (d, *J* = 8.8 Hz, 1H), 5.31 (dd, *J* = 9.6, 8.2 Hz, 1H), 4.29 (dd, *J* = 9.0, 8.3 Hz, 1H), 4.23 (dd, *J* = 12.2, 4.9 Hz, 1H), 4.19-4.13 (m, 2H), 3.95 (ddd, *J* = 9.4, 4.9, 4.2 Hz, 1H), 2.08 (s, 3H), 0.83 (s, 9H), 0.24 (s, 3H), -0.16 (s, 3H).



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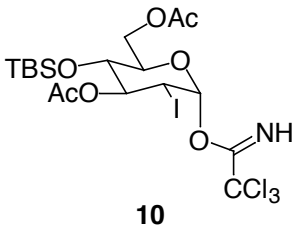
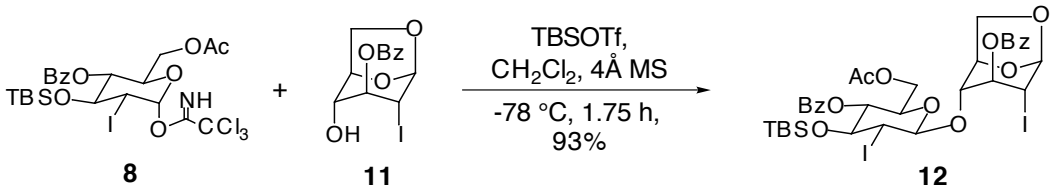
6-O-Acetyl-3-O-(*tert*-butyldimethyl)silyl-2-deoxy-2-iodo-4-O-pivaloyl-1-trichloroacetimido-α-D-glucopyranose (9). $[\alpha]_D^{23}$ +62.6° (*c* 3.0, C_6H_6); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (s, 1 H), 6.48 (d, *J* = 3.3 Hz, 1 H), 5.11 (dd, *J* = 11.0, 8.0 Hz, 1 H), 4.29 (app t, J = 9.0 Hz, 1H), 4.0-4.2 (m, 3 H), 2.04 (s, 3H), 1.23 (s, 9H), 0.92 (s, 9 H), 0.28 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175, 169, 167.9, 160.3, 97.5, 94.7, 77.4, 73.3, 71.0, 62.1, 36.6, 31.6, 27.5, 27.4, 26.3, 22.6, 20.7, 14.1, -2.9, -3.2; IR (thin film from C_6H_6) 3345, 2957, 2857, 1739, 1675, 1623, 1251 cm^{-1}.



10

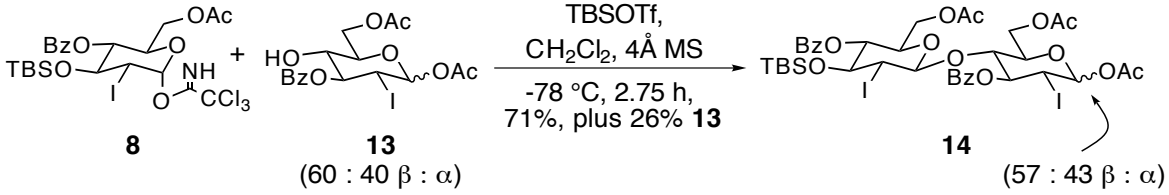
3,6-Di-O-acetyl-4-O-(*tert*-butyldimethyl)silyl-2-deoxy-2-iodo-1-trichloroacetimido-α-D-glucopyranose (10). $[\alpha]_D^{23}$ +46.8° (*c* 3.1, C_6H_6); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.75 (s, 1 H), 6.41 (d, *J* = 3.2 Hz, 1 H), 5.55 (dd, *J* = 10.0, 9.0 Hz, 1 H), 4.0-4.4 (m, 3 H), 3.86 (dd, *J* = 8.0, 9.0 Hz, 1 H), 2.15 (s, 3H), 2.0 (s, 3H), 0.84 (s, 9 H), 0.05 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175, 170, 169, 167, 160.5, 95.6, 94.7, 73.1, 70.0, 62.3, 26.0, 25.6, 23.8, 21.8, 20.8, 17.8, -4.1, -4.2; IR (thin film from C_6H_6) 3441, 3349, 3217, 2956, 2930, 2859, 1741, 1672, 1626, 1254 cm^{-1}; HRMS (FAB), calcd for $C_{18}H_{29}O_7NISiCl_3Na$ (M+Na): 653.9723, found 653.9724.



4-O-(6-O-Acetyl-4-O-benzoyl-3-O-(*tert*-butyldimethyl)silyl-2-deoxy-2-iodo-β-D-glucopyranosyl)-1:6-Anhydro-3-O-benzoyl-2-deoxy-2-iodo-D-glucopyranose (12). A mixture of α-gluco-imidate **8** (3.61 g, 5.20 mmol), acceptor **11** (1.30 g, 3.46 mmol), and 4Å molecular sieves (260 mg) in CH_2Cl_2 (17.3 mL) was stirred for 5 min at 23 °C and then cooled to -78 °C. To this mixture was added TBSOTf (40 μL, 0.17 mmol). The mixture was stirred for 1.75 h at -78 °C, the Et_3N (30 μL) was added, the cooling bath was removed, and CH_2Cl_2 and saturated aqueous $NaHCO_3$ were added. The mixture was stirred vigorously for several minutes and then the layers were separated. The aqueous layer was extracted twice with CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated to yield crude material as a cloudy, orange oil. This oil was dissolved in a solution of 1 : 9, CH_2Cl_2 : hexanes, causing a white solid to crash out of solution. This mixture was filtered through a plug of glass wool to remove the solid, and the solid was washed with a 1 : 9

mixture of CH_2Cl_2 and hexanes. The filtrate was concentrated to yield 5.1 g of an orange oil. This crude material was purified by flash chromatography on 250 g of silica gel to afford 3.26 g of a yellow oil that contained the desired β-disaccharide **12** contaminated with trichloroacetamide. Based on the ^1H NMR spectrum and integration ratios, the mixture was determined to contain the desired β-disaccharide **12** (2.92 g, 93%) and trichloroacetamide (0.34 g). This material was used directly in a subsequent experiment (acetolysis of the anhydro linkage). HPLC separation of mixed fractions afforded small amounts of the α-*gluco*- and α–*manno* diastereomers of **12**.

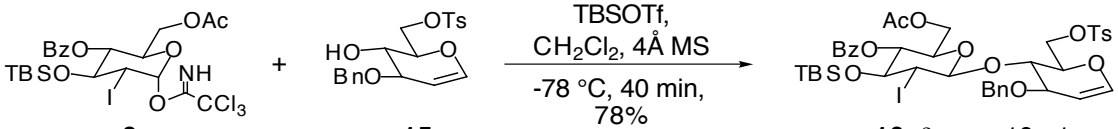
Data for β-*gluco*-disaccharide **12**: $[\alpha]_D^{24}$ +35.8° (c 4.21, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ 8.03-8.01 (m, 4H), 7.62-7.57 (m, 2H), 7.49-7.44 (m, 4H), 5.87 (s, 1H), 5.78 (s, 1H), 5.20 (dd, *J* = 9.8, 8.5 Hz, 1H), 5.04 (d, *J* = 9.0 Hz, 1H), 4.84 (d, *J* = 5.6 Hz, 1H), 4.25-4.18 (m, 3H), 4.15 (dd, *J* = 12.0, 5.9 Hz, 1H), 4.10, 4.08 (AB system, *J* = 9.5 Hz, 2H), 3.91 (ddd, *J* = 9.8, 5.7, 3.9 Hz, 1H), 3.88 (dd, *J* = 7.6, 5.9 Hz, 1H), 3.75 (s, 1H), 1.85 (s, 3H), 0.82 (s, 9H), 0.23 (s, 3H), -0.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 165.4, 164.8, 133.7, 133.4, 129.8, 129.7, 129.6, 129.0, 128.6, 128.5, 104.8, 102.7, 78.6, 77.2, 74.1, 72.9, 72.3, 65.6, 63.0, 36.2, 26.1, 20.6, 20.2, 18.2, -3.2, -3.4; IR (thin film from $CDCl_3$): 3064, 2958, 2929, 2898, 2857, 2254, 1916, 1732, 1602, 1585, 1492, 1472, 1463, 1452, 1369, 1339, 1314, 1296, 1267, 1177, 1114, 1069, 1026, 1002, 968, 944, 909, 837, 779, 731, 711 cm^{-1}; HRMS calcd for $C_{34}H_{42}O_{11}I_2SiNa$ (M+Na) 931.0487, found 931.0440. Anal. Calcd for $C_{34}H_{42}O_{11}I_2Si$: C, 44.95; H, 4.66. Found C, 44.74; H, 4.89.



Acetyl 4-O-(6-O-Acetyl-4-O-benzoyl-3-O-(*tert*-butyldimethyl)silyl-2-deoxy-2-iodo-β-D-glucopyranosyl)-6-O-acetyl-3-O-benzoyl-2-deoxy-2-iodo-β-D-glucopyranoside (14): $[\alpha]_D^{24}$ +26.8° (c 3.49, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ 8.10-8.08 (m, 2H), 7.94-7.93 (m, 2H), 7.62-7.54 (m, 2H), 7.49-7.40 (m, 4H), 5.93 (d, *J* = 9.5 Hz, 1H), 5.61 (br s, 1H), 4.78 (dd, *J* = 9.0, 8.8 Hz, 1H), 4.64-4.62 (m, 3H), 4.14-4.10 (m, 1H), 4.06 (dd, *J* = 9.5,

8.5 Hz, 1H), 4.02-3.98 (m, 2H), 3.69 (app t, *J* = 9.3 Hz, 1H), 3.60 (dd, *J* = 11.5, 5.6 Hz, 1H), 3.54-3.48 (m, 2H), 2.16 (s, 3H), 2.14 (s, 3H), 1.73 (s, 3H), 0.77 (s, 9H), 0.16 (s, 3H), -0.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 170.0, 168.4, 165.3, 165.0, 133.44, 133.43, 129.80, 129.76, 129.6, 128.5, 101.4, 94.0, 75.4, 74.8, 74.0, 73.4, 72.2, 63.2, 62.7, 34.1, 26.3, 26.0, 20.8, 20.7, 20.4, 18.2, -3.2, -3.6; IR (thin film from $CDCl_3$): 3065, 2956, 2931, 2892, 2857, 1738, 1602, 1472, 1461, 1452, 1368, 1315, 1268, 1254, 1234, 1177, 1110, 1068, 1027, 838, 779, 710 cm^{-1}; HRMS calcd for $C_{38}H_{48}O_{14}I_2SiNa$ (M+Na) 1033.0804, found 1033.0762.

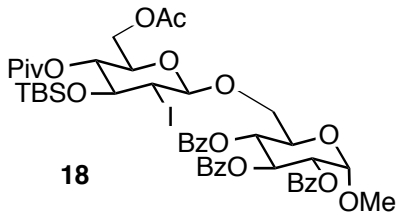
Partial data for α-acetate anomer of disaccharide **14**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09-8.08 (m, 2H), 7.93-7.92 (m, 2H), 7.61-7.54 (m, 2H), 7.49-7.46 (m, 2H), 7.43-7.40 (m, 2H), 6.36 (d, *J* = 3.2 Hz, 1H), 5.75 (br s, 1H), 4.79 (app t, *J* = 8.6 Hz, 1H), 4.66 (dd, *J* = 12.4, 3.9 Hz, 1H), 4.63 (d, *J* = 9.0 Hz, 1H), 4.55 (dd, *J* = 12.2, 1.5 Hz, 1H), 4.26-4.22 (m, 2H), 4.06 (dd, *J* = 9.3, 8.8 Hz, 1H), 4.02 (m, 1H), 3.71 (app t, *J* = 9.3 Hz, 1H), 3.61-3.57 (m, 1H), 3.50-3.45 (m, 2H), 2.24 (s, 3H), 2.13 (s, 3H), 1.68 (s, 3H), 0.77 (s, 9H), 0.17 (s, 3H), -0.25 (s, 3H).



4-O-(6-O-Acetyl-4-O-benzoyl-3-O-(*tert*-butyldimethyl)silyl-2-deoxy-2-iodo-β-D-glucopyranosyl)-3-O-benzyl-2-deoxy-6-O-*p*-toluenesulfonyl-D-*arabino*-hex-1-enitol (16): $[\alpha]_D^{27}$ +40.2° (c 1.07, CH_2Cl_2); ^{1}H NMR (500 MHz, C_6D_6) δ 8.09-8.07 (m,2H), 7.80-7.78 (m, 2H), 7.31-7.29 (m, 2H), 7.21-7.18 (m, 2H), 7.13-7.04 (m, 4H), 6.70-6.68 (m, 2H), 6.08 (dd, *J* = 6.2, 0.8 Hz, 1H), 5.25 (dd, *J* = 10.0, 8.5 Hz, 1H), 4.67 (d, *J* = 9.3 Hz, 1H), 4.68-4.62 (m, 2H), 4.50 (dd, *J* = 11.0, 3.7 Hz, 1H), 4.47-4.44 (m, 1H), 4.40 (s, 2H), 4.14-4.11 (m, 3H), 4.03 (app t, *J* = 3.9 Hz, 1H), 4.00 (dd, *J* = 9.9, 8.4 Hz, 1H), 3.70 (dd, *J* = 9.8, 9.3 Hz, 1H), 3.29 (app dt, *J* = 9.8, 4.2 Hz, 1H), 1.83 (s, 3H), 1.62 (s, 3H), 0.92 (s, 9H), 0.29 (s, 3H), -0.09 (s, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 169.8, 165.4, 144.4, 144.2, 139.0, 133.4, 130.1, 129.9, 128.7, 128.6, 128.34, 128.29, 127.9, 127.8, 127.7, 102.4, 99.7, 77.5, 73.8, 73.6, 73.2, 72.4, 71.7, 70.1, 68.2, 62.8, 35.7, 26.4,

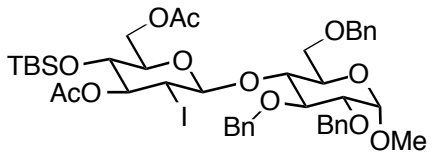
21.2, 20.2, 18.5, -2.7, -3.1; IR (thin film from C_6D_6): 3066, 3032, 2956, 2930, 2885, 2858, 1732, 1650, 1600, 1496, 1472, 1452, 1367, 1267, 1190, 1178, 1117, 1097, 1068, 1027, 981, 960, 838, 816, 780, 737, 712, 667 cm^{-1}.

Partial ^1H NMR data for α-*gluco*-diastereomer of **16** determined from mixed fractions: ^1H NMR (500 MHz, C_6D_6) δ 8.20-8.18 (m, 2H), 7.74-7.73 (m, 2H), 7.27-7.04 (m, 8H), 6.64-6.62 (m, 2H), 6.03 (dd, *J* = 6.2, 0.9 Hz, 1H), 5.37 (dd, *J* = 10.1, 8.8 Hz, 1H), 5.09 (d, *J* = 3.4 Hz, 1H), 4.19 (dt, *J* = 11.1, 3.0 Hz, 1H), 4.11 (app t, *J* = 3.9 Hz, 1H), 3.86 (app t, *J* = 4.3 Hz, 1H), 3.57 (dd, *J* = 10.4, 3.3 Hz, 1H), 1.83 (s, 3H), 1.77 (s, 3H), 0.99 (s, 9H), 0.30 (s, 3H), -0.10 (s, 3H).



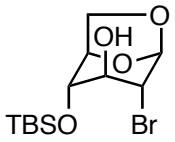
18

Methyl 6-O-(6-O-Acetyl-3-O-(*tert*-butyldimethyl)silyl-2-deoxy-2-iodo-4-O-pivaloyl-β-D-glucopyranosyl)-2,3,4-tri-O-benzoyl-α-D-glucopyranoside (18): $[\alpha]_D^{24}$ +59.3° (c 6.0, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ 7.8-8.0 (m, 6H), 7.2 -7.6 (m, 9H), 6.14 (app t, *J* = 9.6 Hz, 1H), 5.52 (app t, *J* = 9.8 Hz, 1H), 5.27 (dd, *J* = 9.2, 3.6 Hz, 1H), 5.25 (d, *J* = 3.6 Hz, 1H), 4.88 (dd, *J* = 7.7, 8.8 Hz, 2H), 4.71, (d, *J* = 8.8 Hz, 1H), 4.32 (m, 1H), 4.0-4.2 (m, 4H), 3.79 (m, 2 H), 3.6 (m, 1H), 3.53 (s, 3H), 2.00 (s, 3H), 1.2 (s, 9H), 0.89 (s, 9H), 0.2 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.2, 170.7, 165.7, 165.8, 165.4, 133.4, 133.3, 133.0, 129.9, 129.8, 129.6, 129.2, 129.0, 128.4, 128.9, 127.7, 128.3, 128.2, 103.5, 96.8, 77.7, 72.9, 72.0, 71.9, 70.4, 69.8, 68.9, 68.7, 62.7, 55.9, 39.1, 33.9, 29.6, 27.3, 26.2, 20.6, 18.3, -3.2, -3.3; IR (thin film from CH_2Cl_2): 2930, 2958, 2857, 1732 cm^{-1}; HRFAB MS calcd for $C_{47}H_{59}O_{15}ISiNa$ (M+Na): 1041.2567, found 1041.2589.



19

Methyl 4-O-(3,6-Di-O-acetyl-4-O-(*tert*-butyldimethyl)silyl-2-deoxy-2-iodo-β-D-glucopyranosyl)-2,3,6-tri-O-benzyl-α-D-glucopyranoside (19): $[\alpha]_D^{24}$ +42° (c 1.6, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.2-7.4 (m, 15H), 4.92, 4.7 (AB system, *J* = 11.7 Hz, 2H), 4.75 (AB system, *J* = 12.7 Hz, 2H), 4.41, 4.56 (AB system, *J* = 11.5 Hz, 2H), 4.39 (d, *J* = 9.7 Hz, 1H), 4.23 (dd, *J* = 12, 0.6 Hz, 1H), 4.16 (dd, *J* = 10.9, 1.0 Hz, 1H), 3.96 (app t, *J* = 9.5 Hz, 1H), 3.83 (dd, *J* = 12.0, 0.5 Hz, 1H), 3.81 (app t, *J* = 9.2 Hz, 1H), 3.72 (m, 1H), 3.62 (dd, *J* = 10.0, 9.0 Hz, 1H), 3.52 (dd, *J* = 9.3, 8.7 Hz, 1H), 3.48 (dd, *J* = 5.9 Hz, 1H), 3.38 (s, 3H), 2.9 (m, 1H), 2.13 (s, 3H), 1.88 (s, 3H), 0.86 (s, 9H), 0.03 (s, 3H), -0.02 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 169, 139.6, 138.3, 137.8, 128.81, 128.4, 128.58, 128.45, 128.29, 128.09, 128.01, 127.73, 127.18, 127.02, 100.3, 98.3, 80.2, 78.8, 75, 74, 73.8, 73.45, 73.30, 70, 69.4, 68.7, 62, 55.3, 31.0, 25.8, 21.7, 20, 17.1, -4.1, -4.2; IR (thin film from CH_2Cl_2): 2929, 2858, 1727 cm^{-1}; HRFAB MS calcd for $C_{44}H_{59}O_{12}ISiNa$ (M+Na): 957.2720, found 957.2720.



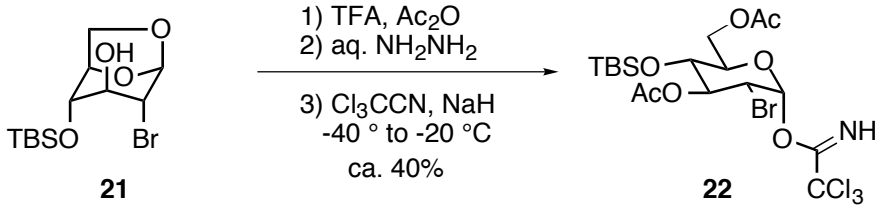
21

1:6-Anhydro-4-O-(*tert*-butyldimethyl)silyl-2-deoxy-2-bromo-D-glucopyranoside (21). To a solution of 10 g (0.037 mol) of triacetyl D-glucal in 105 mL of methanol was added catalytic amount (~25 mg) of sodium metal. The mixture was stirred for 25 min at 23 °C, at which point TLC analysis indicated the absence of the starting material. The reaction mixture was neutralized to pH 7 by the addition of dry ice. Methanol was removed under reduced pressure and the residue methanol was co-evaporated with ethyl acetate. The resulting residue was placed under high vacuum overnight.

The resulting solid was mixed with 250 mL of acetonitrile, 16.5 g (0.028 mol) of $(Bu_3Sn)_2O$, and 10 g of 3 Å molecular sieves. The mixture was heated for 30 min at reflux and the heating mantle was removed. *N*-Bromosuccinimide (9.9 g, 0.056 mol) was added at 0 °C and the resulting mixture was

stirred for 5 h at 23 °C. The reaction mixture was filtered through Celite and the filtrate was evaporated to near dryness. Hexanes and an aqueous solution of $Na_2S_2O_3$ (165 mL of each) were added to the residue and stirred for 3 h at 23 °C. The layers were separated and the aqueous layer was continuously extracted for 16 h with ethyl acetate using a liquid-liquid extractor. The solvent of the organic extracts was removed under reduced pressure to give the desired 1:6-anhydro-2-deoxy-2-bromo-glucopyranose as a solid (10.6 g, 68%). This crude mixture was contaminated by succinimide and was used in the next reaction without further purification.

The crude anhydro sugar (8.5 g, 17 mmol) was dissolved in 68 mL of DMF. To this solution was added 8.1 g (119 mmol) of imidazole and 3.6 g (23.8 mmol) of *t*-butyldimethylsilyl chloride at 0 °C. The mixture was stirred for 3 h at 23 °C. Ether and sat. $NaHCO_3$ solution (200 mL each) were added to the reaction mixture. The resulting mixture was vigorously stirred for 40 min, the layers were separated, and the aq. solution was extracted with ether (2 x 100 mL). The combined organic layers were washed with brine, dried over $MgSO_4$. After removing the solvent under reduced pressure, the residue was purified by column chromatography to yield 4.2 g (73%) of the desired anhydro sugar **21** as an oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.6 (s, 1H), 4.44 (d, *J* = 5.1 Hz, 1H), 4.1 (d, *J* = 7.0 Hz, 1H), 3.90 (b, 1H), 3.74 (d, J = 2.9 Hz, 1 H), 3.72 (dd, J = 5.1, 7.3 Hz, 1H), 3.65 (dd, J = 1.7, 2.7 Hz, 1H), 2.4 (b, 1H), 0.93 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 102.4, 77.8, 75.1, 73.4, 66.2, 48.4, 25.7, 18.0, -4.8, -4.9; IR (thin film): 3480, 2929, 2898, 2858 cm^{-1}; HRMS calcd for $C_{12}H_{24}O_4{}^{79}BrSi$ (M+ H) 339.0627, found 339.0615.



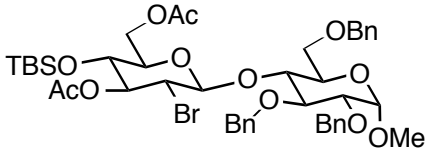
3,6-Di-O-acetyl-4-O-(*tert*-butyldimethyl)silyl-2-deoxy-2-bromo-1-trichloroacetimido-α-D-glucopyranose (22). To a solution of 2.1 g (6.2 mmol) of the bromoanhydro sugar (**21**) in 30 mL of acetic anhydride at 23 °C was added 0.95 mL (12.4 mmol) of trifluoroacetic acid. The solution was stirred at 23 °C for 2 h and then 150 mL of ethyl acetate was

added. The resulting mixture was added dropwise to a sat. sodium bicarbonate solution with care. Solid sodium bicarbonate was added to the solution till the evolution of carbon dioxide stops. The layers were separated and the aq. layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over magnesium sulfate, and filtered. After removing the solvent under reduced pressure, the residue was identified as a mixture of β/α anomers (2:1) of acetyl 3,6-O-diacetyl-2-deoxy-2-bromo-4-O-t-butyldimethyl-D-glucopyranoside. The mixture was used directly in the next step without any further purification: ^{1}H NMR data for the β-isomer (500 MHz, $CDCl_3$): 5.80 (d, J = 9.2 Hz, 1H), 5.28 (app t, J = 10.6 Hz, 1H), 4.40 (dd, J = 2.2, 12.5 Hz, 1H), 4.10 (m, 2H), 3.80 (m, 2H), 2.15 (s, 3H), 2.14 (s, 3H), 2.08 (s, 3H), 0.84 (s, 9H), 0.04 (s,3H), 0.03 (s, 3H).

The triacetyl sugar was dissolved in 60 mL of methanol and 1.1 mL of an 11 M aq. hydrazine was added. The reaction mixture was stirred for 2 h at 23 °C and was then poured into a 150 mL water/150 mL ethyl acetate mixture. The mixture was shaken to allow the partition of the product between the organic and the aq. layers. The layers were separated and the aq. layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over magnesium sulfate, and filtered. After removing the solvents under reduced pressure, the residue was purified by column chromatography (EtOAc/Hex, 1:3) to yield 1.42 g (66%) of the lactol as a foaming oil (β/α ratio = 1:1.35). ^{1}H NMR data for diagnostic protons (500 MHz, $CDCl_3$): β-anomer, 5.24 (dd, J = 8.5, 10.7 Hz, 1H, C3H), 4.92 (d, J = 8.5 Hz, 1H, C1H); α-anomer, 5.52 (dd, J = 8.8, 11.0 Hz, 1H, C3H), 5.38 (d, J = 2.4 Hz, 1H, C1H).

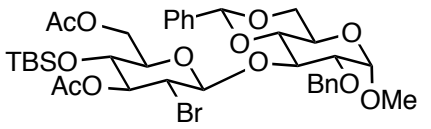
A solution of the lactol (1.4 g, 3.2 mmol) in trichloroacetonitrile (32 mL) at -40 °C was treated with NaH (1 g, 25 mmol). The reaction mixture was stirred at -40 °C for 1 h, allowed to warm to -20 °C, and was then placed in a -20 °C freezer overnight. The reaction mixture was filtered through Celite to remove the NaH, and the Celite was washed with EtOAc. The filtrate was washed with brine (50 mL) and the brine layer was extracted with CH_2Cl_2 (50 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated to give a ca. 5:1 (α:β) mixture of anomeric trichloroacetimidates. Purification of the crude product by column chromatography on Davisil silica gel (hexanes/ethyl acetate, 10:1) furnished the α-trichloroacetimidate **22** (1.1 g, 59 %) as an oil: $[\alpha]_D^{23}$ +101.6° (*c* 2.9, C_6H_6); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.7 (s, 1 H), 6.5 (d, *J* = 3.5 Hz, 1 H), 5.5 (dd,

J = 10.7, 8.8 Hz, 1 H), 4.4 (d, *J* = 9.9 Hz, 1 H), 4.1-4.15 (m, 3 H), 3.86 (dd, *J* = 8.7, 9.4 Hz, 1 H), 2.15 (s, 3H), 2.07 (s, 3H), 0.86 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.4, 169.5, 160.6, 128.3, 94.5, 73.8, 72.9, 70.0, 62.2, 46.8, 25.6, 21.4, 17.8, -4.1, -4.2; IR (film from CH_2Cl_2) 3346, 3218, 2958, 2859, 1747, 1674 cm^{-1}; HRMS (FAB), calcd for $C_{18}H_{29}O_7NSi^{79}BrCl_3Na$ (M+Na): 605.9859, found 605.9851, 607.9819.



23

Methyl 4-O-(3,6-Di-O-acetyl-2-bromo-4-O-(*tert*-butyldimethyl)silyl-2-deoxy-β-D-glucopyranosyl)-2,3,6-tri-O-benzyl-α-D-glucopyranoside (23): $[\alpha]_D^{24}$ +39.3° (c 1.5, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.23 (m, 15H), 5.28 (app t, *J* = 8.8 Hz, 1H), 5.1, 4.8 (AB system, *J* = 12 Hz, 2H), 4.56, 4.27 (AB system, *J* = 12.2 Hz, 2H), 4.48, 4.18 (AB system, *J* = 12.0 Hz, 2H), 4.75 (d, *J* = 8.5 Hz, 1H), 4.61 (d, *J* = 3.4 Hz, 1H), 4.37 (dd, *J* = 11.0, 7.8 Hz, 1H), 4.34 (dd, *J* = 10.9, 6.2 Hz, 1H), 4.19 (dd, 1H), 3.97 (dd, *J* = 10.9, 1.8 Hz, 1H), 3.7 (d, 1H), 3.66 (dd, *J* = 3.9 Hz, 1H), 3.54 (dd, 1H), 3.5 (m, 1H), 3.10 (s, 3H), 3.05 (m, 1H), 1.8 (s, 3H), 1.6 (s, 3H), 0.97 (s, 9H), -0.04 (s, 3H), -0.06 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.0, 139.2, 138.1, 137.0, 128.73, 128.47, 128.34, 128.31, 128.1, 128.05, 128.0, 127.75, 127.07, 100.2, 98.0, 80.1, 78, 75.9, 74.8, 73.7, 73.5, 70.1, 69.4, 68.3, 55.3, 51.8, 29.7, 25.6, 21.4, 20.7, 17.8, -4.1, -4.2; IR (thin film from CH_2Cl_2): 2954, 2930, 2858, 1745 cm^{-1}; HRMS(FAB) calcd for $C_{44}H_{59}O_{12}NaSi^{79}Br$ (M+Na) 909.2857, found 909.2900, 911.2892.



25

Methyl 3-O-(3,6-Di-O-acetyl-2-bromo-4-O-(*tert*-butyldimethyl)silyl-2-deoxy-β-D-glucopyranosyl)-2-O-benzyl-4,6-O-benzylidene-α-D-glucopyranoside (25): $[\alpha]_D^{28}$ +34° (c 1.2, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53-7.30 (m, 10H), 5.43 (s, 1H), 5.1 (dd, 1H),

4.85-4.50 (AB system, *J* = 12.2 Hz, 2H), 4.92 (d, *J* = 8.6 Hz, 1H), 4.33 (d, *J* = 3.9 Hz, 1H), 4.2 (app t, *J* = 5.0 Hz, 1H), 4.1 (app t, 1H), 3.8 (dd, *J* = 11.9 Hz, 1H), 3.74 (m, 1H), 3.72 (dd, J =10.7, 8.7 Hz, 1H), 3.61 (dd, J = 10.5, 9.0 Hz, 1H), 3.53 (dd, *J* = 9.3, 3.9 Hz, 1H), 3.49 (app t, J = 9.4 Hz, 1H), 3.22 (s, 3H), 2.05 (s, 3H), 1.87 (s, 3H), 0.73 (s, 9H), -0.08 (s, 3H), -0.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 169.7, 138.1, 137.2, 129.1, 128.5, 128.4, 128.2, 128.1, 126.2, 101.7, 101.5, 98.7, 79.9, 79.8, 77.2, 76.9, 74.3, 74.0, 70.1, 68.9, 62.6, 61.9, 55.3, 51.3, 42.9, 29.7, 25.5, 21.5, 20.8, 17.7, -4.2, -4.1; IR (solution in $CDCl_3$): 2931, 2859, 1738 cm^{-1}; HRMS(FAB) calcd for $C_{37}H_{51}O_{12}NaSi^{79}Br$ 817.2231, found 817.2264, 819.2259.