SUPPORTING INFORMATION

C2-Hydroxyglycosylation with Glycal Donors. Probing the Mechanism of Sulfonium-Mediated Oxygen Transfer to Glycal Enol Ethers.

*Eiji Honda and David Y. Gin**

Department of Chemistry, University of Illinois at Urbana-Champaign, Urbana, IL 61801
gin@scs.uiuc.edu

General Procedures. All reactions were performed in flame-dried modified Schlenk (Kjeldahl shape) flasks fitted with a glass stopper or rubber septa under a positive pressure of argon, unless otherwise noted. Low temperature NMR experiments were performed in 5 mm NMR tubes (dried under a stream of N_2 gas) topped with a rubber septa under a positive pressure of argon. Air- and moisture-sensitive liquids and solutions were transferred via syringe or stainless steel cannula. Organic solutions were concentrated by rotary evaporation below 30 °C at *ca.* 25 Torr. Flash column chromatography was performed employing 230-400 mesh silica gel. Thin-layer chromatography (analytical and preparative) was performed using glass plates pre-coated to a depth of 0.25 mm with 230-400 mesh silica gel impregnated with a fluorescent indicator (254 nm).

Materials. Dichloromethane, diisopropylethylamine, triethylamine, and acetonitrile were distilled from calcium hydride at 760 Torr. CD_2Cl_2 was stored over CaH_2 and vacuum transferred immediately prior to use. Methyl alcohol was distilled from Mg/I_2. ^{18}O-Labeled diphenyl sulfoxide ($Ph_2S^{18}O$), and ^{18}O-labeled dibenzothiophene oxide ($DBT^{18}O$) were prepared following literature procedures.[1] Trifluoromethanesulfonic anhydride (Tf_2O) was triply distilled from phosphorous pentoxide.

Instrumentation. Infrared (IR) spectra were obtained using a Perkin-Elmer Spectrum BX spectrophotometer referenced to polystyrene standard. Data are presented as frequency of

absorption (cm^{-1}). Proton and carbon-13 nuclear magnetic resonance (^{1}H NMR or ^{13}C NMR) spectra were recorded on a Varian 500, and a Varian Inova 500 NMR spectrometer; chemical shifts are expressed in parts per million (δ scale) downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CHCl_3$, δ_H 7.26; $CHDCl_2$, δ_H 5.32; $CDCl_3$, δ_C 77.0; CD_2Cl_2, δ_C 53.8). Data are presented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet and/or multiple resonances), integration, coupling constant in Hertz (Hz) and assignment. Melting points were recorded with a Fisher melting point apparatus and are uncorrected.

***tert*-Butyl 3,4,6-tri-*O*-benzyl-β-D-glucopyranoside.** Colorless oil: R_f= 0.22 (17% ethyl acetate in hexane); $[\alpha]_D^{20}$ = –5.9 (c = 1.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.18 (m, 15 H), 4.97 (d, 1H, *J* = 11.1 Hz), 4.85 (d, 1H, *J* = 11.1 Hz), 4.83 (d, 1H, *J* = 11.2 Hz), 4.60 (d, 1H, *J* = 12.0 Hz), 4.55 (d, 1H, *J* = 11.0 Hz), 4.54 (d, 1H, *J* = 12.1 Hz), 4.43 (d, 1H, *J* = 8.72 Hz, H1), 3.72 (dd, 1H, *J* = 10.7 and 1.9 Hz), 3.65 (dd, 1H, *J* = 10.8 and 5.1 Hz), 3.56 (t, 1H, *J* = 9.2 Hz), 3.51 (dd, 1H, *J* = 8.8 and 8.0 Hz), 3.49 (ddd, 1H, *J* = 9.9 and 5.1 and 1.9 Hz), 2.25 (bs, 1H,), 1.31 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.90, 138.42, 138.34, 128.52, 128.49, 128.24, 128.05, 127.83, 127.77, 127.74, 127.62, 97.41, 84.94, 77.81, 76.28, 75.05, 75.04, 74.96, 73.44, 69.37, 28.92; FTIR (neat film) 3499, 3087, 3062, 3029, 2976, 2905, 2870, 1495, 1455, 1364, 1112, 1062 cm^{-1}; HRMS (FAB) *m/z*: Calcd for $C_{31}H_{37}O_6$ (M-H) 505.2590, found 505.2593.

Benzyl 3,4,6-tri-*O*-benzyl-β-D-glucopyranosylamine. White solid: mp 123-124 ºC (from ethanol) (lit: 117-119 ºC); R_f= 0.28 (30% ethyl acetate in hexane); $[\alpha]_D^{20}$ = –11.0 (c = 1.34, $CHCl_3$) (lit: $[\alpha]_D^{20}$ = –7.13, c = 2.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.27 (m, 18H), 7.16-7.15 (m, 2H), 4.98 (d, 1H, *J* = 11.3 Hz), 4.85 (d, 1H, *J* = 10.8 Hz), 4.82 (d, 1H, *J* = 11.3 Hz), 4.66 (d, 1H, *J* = 12.3 Hz), 4.56 (d, 1H, *J* = 12.2 Hz), 4.51 (d, 1H, *J* = 10.8 Hz), 4.14 (d, 1H, *J* = 13.4 Hz), 3.88 (d, 1H, *J* = 13.2 Hz), 3.88 (d, 1H, *J* = 8.4 Hz, H1), 3.77-3.71 (m, 2H),

3.67-3.58 (m, 2H), 3.45-3.42 (m, 1H), 3.38 (t, 1H, *J* = 8.5 Hz), 2.69 (bs, 1H), 1.97 (bs, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 139.61, 138.81, 138.27, 138.07, 128.49, 128.40, 128.37, 128.28, 127.99, 127.91, 127.90, 127.70, 127.69, 127.61, 127.20, 89.76, 85.58, 77.43, 76.24, 74.99, 74.90, 74.88, 73.55, 68.86, 49.54; FTIR (neat film) 3527, 3279, 3063, 3032, 2900, 2865, 1496, 1451, 1398, 1348, 1314, 1258, 1210, 1122, 1064, 1019, 843 cm^{-1}; HRMS (FAB) *m/z*: Calcd for $C_{34}H_{38}NO_5$ (M+H) 540.2750, found 540.2751.

Methyl *O*-(3,4,6-tri-*O*-benzyl-β-D-glucopyranosyl)-(1→6)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside. White solid: mp 135-136 ºC (from methanol-benzene); R_f = 0.40 (20% ethyl acetate in benzene); $[\alpha]_D^{20}$ = +14.0 (c = 1.17, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.26 (m, 28H), 7.19-7.15 (m, 2H), 4.98 (d, 1H, *J* = 10.8 Hz), 4.91 (d, 1H, *J* = 11.1 Hz), 4.89 (d, 1H, *J* = 10.7 Hz), 4.82 (d, 1H, *J* = 11.1 Hz), 4.82 (d, 1H, *J* = 10.8 Hz), 4.81 (d, 1H, *J* = 11.1 Hz), 4.78 (d, 1H, *J* = 13.8 Hz), 4.66 (d, 1H, *J* = 12.2 Hz), 4.61 (d, 1H, *J* = 11.5 Hz), 4.61 (d, 1H, *J* = 3.2 Hz, H1'), 4.58 (d, 1H, *J* = 12.4 Hz), 4.52 (d, 1H, *J* = 9.8 Hz), 4.52 (d, 1H, *J* = 12.6 Hz), 4.23 (d, 1H, *J* = 7.2 Hz, H1), 4.15 (dd, 1H, *J* = 10.9 and 2.2 Hz), 4.00 (t, 1H, *J* = 9.3 Hz), 3.84-3.80 (m, 1H), 3.72 (dd, 1H, *J* = 11.0 and 1.9 Hz), 3.70-3.65 (m, 2H), 3.57-3.48 (m, 5H), 3.46-3.43 (m, 1H), 3.37 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.70, 138.62, 138.24, 138.17, 138.08, 138.06, 128.50, 128.45, 128.42, 128.41, 128.36, 128.17, 128.00, 127.97, 127.94, 127.84, 127.79, 127.77, 127.73, 127.71, 127.65, 127.59, 103.50, 98.09, 84.45, 81.99, 79.68, 78.01, 77.47, 75.79, 75.33, 75.10, 75.04, 75.02, 74.47, 73.43, 73.38, 69.79, 68.94, 68.78, 55.28; FTIR (neat film) 3472, 3088, 3062, 3030, 2903, 2869, 1497, 1454, 1360, 1090, 1066, 1028 cm^{-1}; HRMS (FAB) *m/z*: Calcd for $C_{55}H_{59}O_{11}$ (M-H) 895.4057, found 895.4056.

Benzyl 3,4,6-tri-*O*-*para*-methoxybenzyl-β-D-glucopyranoside. White solid: mp 104-105 ºC (from ethanol); R_f = 0.24 (30% ethyl acetate in hexane); $[\alpha]_D^{20}$ = –27.8 (c = 0.91, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.27 (m, 9H), 7.09-7.06 (m, 2H), 6.88-6.85 (m, 4H), 6.84-6.81 (m, 2H), 4.95 (d, 1H, *J* = 11.7 Hz), 4.83 (d, 1H, *J* = 11.0 Hz), 4.77 (d, 1H, *J* = 11.2 Hz), 4.74 (d, 1H, *J* = 10.4 Hz), 4.62 (d, 1H, *J* = 11.7 Hz), 4.58 (d, 1H, *J* = 11.8 Hz), 4.49 (d, 1H, *J* = 11.9 Hz), 4.44 (d, 1H, *J* = 10.4 Hz), 4.34 (d, 1H, *J* = 7.5 Hz, H1), 3.80 (s, 3H), 3.79 (s, 3H), 3.78 (s, 3H), 3.71 (dd, 1H, *J* = 10.8 and 2.0 Hz), 3.66 (dd, 1H, *J* = 10.8 and 4.6 Hz), 3.61-3.52 (m, 3H), 3.45 (ddd, 1H, J = 9.2, 4.6 and 2.1 Hz), 2.29 (d, 1H, *J* = 2.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.50, 159.48, 159.45, 137.41, 131.03, 130.49, 130.41, 129.85, 129.81, 129.74, 128.70, 128.35, 128.16, 114.09, 113. 98, 101.93, 84.43, 77.51, 75.44, 74.99, 74.87, 78.81, 73.32, 71.26, 68.62, 55.47, 55.45; FTIR (neat film) 3435, 3069, 3033, 3002, 2918, 2960, 2836, 1612, 1585, 1517, 1464, 1361, 1301, 1250, 1064, 1035 cm^{-1}; HRMS (FAB) *m/z*: Calcd for $C_{37}H_{41}O_9$ (M-H) 629.2751, found 629.2750.

Phenyl 3-*O*-benzyl-4,6-di-*O*-isopropylidene-β-D-glucopyranoside. Viscous oil: R_f = 0.39 (15% ethyl acetate in benzene); $[\alpha]_D^{20}$ = –22.4 (c = 1.35, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41-7.28 (m, 7H), 7.07-7.02 (m, 3H), 4.99 (d, 1H, *J* = 7.6 Hz, H1), 4.93 (d, 1H, *J* = 11.6 Hz), 4.79 (d, 1H, *J* = 11.8 Hz), 3.96 (dd, 1H, *J* = 11.0 and 5.4 Hz), 3.84-3.77 (m, 3H), 3.59 (t, 1H, *J* = 9.0 Hz), 3.40 (dt, 1H, *J* = 9.9 and 5.3 Hz), 2.53 (bs, 1H), 1.50 (s, 3H), 1.45 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.96, 138.61, 129.58, 128.46, 127.92, 127.79, 123.08, 116.93, 101.25, 99.50, 80.72, 74.42, 73.93, 73.88, 67.50, 62.17, 29.13, 19.07; FTIR (neat film) 3479,3063, 3030, 2996, 2886, 1590, 1496, 1318, 1306, 1229, 1157, 1091 cm^{-1}; HRMS (FAB) *m/z*: Calcd for $C_{22}H_{27}O_6$ (M+H) 387.1808, found 387.1811.

Methyl 4-*O*-acetyl-1-*O*-allyl-3-*O*-*tert*-butyldimethylsilyl-D-glucuronate (11). Viscous oil: R_f = 0.41 (17% ethyl acetate in benzene); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.91 (dddd, 1H, *J* = 17.1, 11.8, 6.6, 5.3 Hz), 5.31 (ddd, 1H, *J* = 17.3, 3.1, 1.6 Hz), 5.23 (dq, 1H, *J* = 1.03, 1.3 Hz),

4.98 (dd, 1H, *J* = 10.0, 9.1 Hz), 4.41 (ddt, 1H, *J* = 12.7, 5.2, 1.4 Hz), 4.33 (d, 1H, *J* = 7.9 Hz), 4.09 (ddt, 1H, *J* = 12.6, 6.5, 1.3 Hz), 3.73 (s, 3H), 3.73 (t, 1H, *J* = 9.0 Hz), 3.48 (ddd, 1H, *J* = 9.0, 7.9, 2.7 Hz), 2.38 (d, 1H, *J* = 2.8 Hz), 2.06 (s, 9H), 0.85 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.93, 168.27, 133.53, 118.61, 101.64, 74.70, 74.31, 73.13, 72.32, 70.75, 52.99, 25.84, 21.09, 18.29, -4.11, -4.64; FTIR (neat film) 3518, 2955, 2930, 2888, 2857, 1753, 1373, 1249, 1234, 1114, 1034, 839, 780 cm^{-1}; HRMS (FAB) *m/z*: Calcd for $C_{18}H_{32}O_8SiNa$ (M+Na) 427.1764, found 427.1766.

Isopropyl 3,4,6-tri-*O*-benzyl-β-D-galactopyranoside. Viscous oil: R_f 0.36 (33% ethyl acetate in hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.23 (m, 15H, ArH), 4.89 (d, 1H, *J* = 11.4 Hz, benzylic-H), 4.73 (d, 1H, *J* = 11.9 Hz, benzylic-H), 4.69 (d, 1H, *J* = 11.8 Hz, benzylic-H), 4.62 (d, 1H, *J* = 11.4 Hz, benzylic-H), 4.47 (d, 1H, *J* = 11.4 Hz, benzylic-H), 4.43 (d, 1H, *J* = 11.4 Hz, benzylic-H), 4.28 (d, 1H, *J* = 7.7 Hz, H-1), 3.99 (septet, 1H, *J* = 6.3 Hz, C*H*$(CH_3)_2$), 3.94-3.90 (m, 2H), 3.64-3.55 (m, 3H), 3.44 (dd, 1H, *J* = 9.9, 3.0 Hz), 2.31 (d, 1H, *J* = 1.3 Hz, O*H*), 1.25 (d, 3H, *J* = 6.3 Hz, CH(CH_3)$_2$), 1.18 (d, 3H, *J* = 6.3 Hz, CH(CH_3)$_2$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.79, 138.45, 138.16, 128.72, 128.67, 128.59, 128.40, 128.11, 128.03, 127.96, 127.86, 127.78, 101.82, 82.27, 74.71, 73.97, 73.76, 73.21, 72.68, 71.78, 71.60, 69.10, 23.67, 22.04; FTIR (neat film) 3450, 3086, 3061, 3028, 2972, 2921, 2868, 1690, 1495, 1455, 1382, 1100, 1069 cm^{-1}; HRMS (FAB) *m/z*: Calcd for $C_{30}H_{37}O_6$ (M+H) 493.2590, found 493.2590.

3,4,6-Tri-*O*-benzyl-D-[1-^{13}C]-glucal (3a). To a suspension of D-[1-^{13}C]-glucose (**14a**) (151 mg, 0.83 mmol, 1 equiv) in Ac_2O (550 μL, 5.83 mmol, 7 equiv) was added HBr (33% in AcOH, 100 μL, 0.58 mmol, 0.7 equiv), and the mixture was stirred at 23 ºC for 1 h. After 1 h, the reaction mixture was treated with additional HBr (33% in AcOH, 650 μL, 3.76 mmol, 4.5

equiv) and stirred at 23 ºC for 14 h. Sodium acetate (334 mg, 4.07 mmol, 5 equiv) was then added to the reaction, and then resulting reaction mixture was added to a suspension of zinc powder (2.08 g, 31.9 mmol, 38 equiv), $CuSO_4 \cdot 5H_2O$ (53 mg, 0.2 mmol, 0.25 equiv), and NaOAc (1.56 g) in a mixture of H_2O (1.7 mL) and AcOH (2.5 mL). The reaction suspension was stirred vigorously at 23 ºC for 1.5 h, then filtered, and the solid was washed sequentially with ethyl acetate (17 mL) and H_2O (17 mL). The filtrate was partitioned and organic layer was washed sequentially with saturated aqueous $NaHCO_3$ solution (17 mL) and saturated aqueous sodium chloride solution (8 mL). The organic phase was dried (Na_2SO_4) and concentrated to provide a residue of crude tri-acetyl-D-glucal. A mixture of this residue, $PhCH_2Cl$ (3.2 mL, 27.8 mmol, 33 equiv), and powdered KOH (1.152 g, 20.5 mmol, 25 equiv) was vigorously stirred at 110 ºC for 2 h and then cooled to 23 ºC. The reaction mixture was diluted with toluene (9 mL) and H_2O (4.5 mL), partitioned, and the organic layer was washed with H_2O (3 × 4.5 mL). Toluene was removed under reduce pressure at 95 ºC, and the residue was purified by flash column chromatography (9% ethyl acetate in hexane) to afford 3,4,6-tri-*O*-benzyl-D-[1-^{13}C]-glucal (199 mg, 57%) as white needles (from ethyl acetate-hexane), mp 52-53 ºC; R_f = 0.38 (20% ethyl acetate in hexane); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.34-7.27 (m, 15H, ArH), 6.41 (ddd, 1H, $^4J_{H,H}$ = 1.1, $^3J_{H,H}$ = 6.2, $^1J_{C,H}$ = 188.0 Hz, H-1), 4.90 (dt, 1H, $^3J_{H,H}$ = 2.8, 5.8 Hz, $^2J_{C,H}$ = 5.8 Hz, H-2), 4.81 (d, 1H, *J* = 11.2 Hz, benzylic-H), 4.65 (d, 1H, *J* = 11.4 Hz, benzylic-H), 4.63 (d, 1H, *J* = 11.6 Hz, benzylic-H), 4.56 (d, 1H, *J* = 11.8 Hz, benzylic-H), 4.54 (d, 1H, *J* = 11.6 Hz, benzylic-H), 4.53 (d, 1H, *J* = 12.0 Hz, benzylic-H), 4.19-4.16 (m, 1H, H-3), 4.08-4.05 (m, 1H, H-5), 3.822 (dd, 1H, *J* = 6.0, 8.4 Hz, H-4), 3.816 (dd, 1H, *J* = 5.1, 10.9 Hz, H-6), 3.75 (dd, 1H, *J* = 2.8, 10.7 Hz, H-6); ^{13}C NMR (126 MHz, CD_2Cl_2) δ 144.81 (C-1), 139.02, 138.86, 138.68, 128.67, 128.64, 128.22, 128.09, 127.98, 127.92, 127.88, 100.21 (d, $^1J_{C,C}$ = 76.0 Hz, C-2), 77.09

(d, J = 2.8 Hz), 75.70, 74.81 (d, J = 3.8 Hz), 73.89, 73.67, 70.68, 68.98 (d, J = 1.6 Hz); FTIR (neat film) 3030, 2864, 1952, 1871, 1813, 1621, 1496, 1454, 1361, 1233, 1100, 735, 697 cm^{-1}; HRMS (FAB) *m/z*: Calcd for $^{12}C_{39}{}^{13}C_1H_{28}O_4$ (M) 416.1941, found 416.1943.

3,4,6-Tri-*O*-benzyl-D-[2-^{13}C]-glucal (3b). Prepared from D-[2-^{13}C]-glucose (**14b**) in a procedure identical to that for the preparation of **3a**. **3b:** White needles (from ethyl acetate-hexane), mp 52 ºC; R_f = 0.38 (20% ethyl acetate in hexane); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.34-7.26 (m, 15H, ArH), 6.41 (ddd, 1H, $^4J_{H,H}$ = 1.3, $^3J_{H,H}$ = 6.2, $^2J_{C,H}$ = 9.0 Hz, H-1), 4.90 (ddd, 1H, $^3J_{H,H}$ = 2.8, 6.2 Hz, $^1J_{C,H}$ = 165.1 Hz, H-2), 4.81 (d, 1H, J = 11.4 Hz, benzylic-H), 4.65 (d, 1H, J = 11.4 Hz, benzylic-H), 4.63 (d, 1H, J = 11.6 Hz, benzylic-H), 4.56 (d, 1H, J = 11.8 Hz, benzylic-H), 4.54 (d, 1H, J = 11.6 Hz, benzylic-H), 4.52 (d, 1H, J = 12.0 Hz, benzylic-H), 4.19-4.16 (m, 1H, H-3), 4.06 (ddd, 1H, J = 2.8, 5.4, 8.2 Hz, H-5), 3.84-3.81 (m, 1H, H-4), 3.82 (dd, 1H, J = 5.1, 10.7 Hz, H-6), 3.75 (dd, 1H, J = 2.8, 10.7 Hz, H-6); ^{13}C NMR (126 MHz, CD_2Cl_2) δ 144.79 (d, $^1J_{C,C}$ = 74.6 Hz, C-1), 139.02, 138.86, 138.69, 128.67, 128.64, 128.22, 128.09, 127.98, 127.93, 127.88, 100.25 (C-2), 77.09 (d, J = 2.8 Hz), 75.69 (d, J = 46.0 Hz), 74.81, 73.89, 73.67, 70.68 (d, J = 1.8 Hz), 68.99; FTIR (neat film) 3063, 3031, 2866, 1622, 1496, 1454, 1365, 1239, 1102, 736, 697 cm^{-1}; HRMS (FAB) *m/z*: Calcd for $^{12}C_{39}{}^{13}C_1H_{28}O_4$ (M) 416.1941, found 416.1943.

3,4,6-Tri-*O*-d_7-benzyl-D-glucal (d_{21}-3). To the solution of D-glucal (100 mg, 0.68 mmol, 1 equiv) in DMF (4 mL) was added NaH (60% dispersion in mineral oil, 110 mg, 2.74 mmol, 4 equiv) at 0ºC and the reaction was stirred at this temperature for 0.5 h. d_7-Benzyl chloride (268 μL, 2.40 mmol, 3.5 equiv) and TBAI (101 mg, 0.27 mmol, 0.4 equiv) were then added. The ice bath was removed and the reaction mixture was stirred at 23ºC for 4 h. Excess NaH was neutralized with the addition of water (80 mL), and the mixture was extracted with Et_2O (4 × 20

mL) and the combined organic layers were washed with saturated aqueous sodium chloride solution (25 mL), dried (Na_2SO_4), and concentrated, and the residue was purified by flash column chromatography (9% ethyl acetate in hexane) to afford 3,4,6-tri-*O*-d_7-benzyl-D-glucal (244 mg, 82%) as white needles (from ethyl acetate-hexane), mp 48-49 ºC; R_f = 0.38 (20% ethyl acetate in hexane); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 6.41 (dd, 1H, *J* = 1.3, 6.2 Hz, H-1), 4.90 (dd, 1H, *J* = 2.8, 6.2 Hz, H-2), 4.17 (dddd, 1H, *J* = 0.6, 1.5, 2.8, 6.0 Hz, H-3), 4.06 (ddd, 1H, *J* = 2.8, 5.4, 8.1 Hz, H-5), 3.82 (dd, 1H, J = 5.2, 10.9 Hz, H-6), 3.81 (dd, 1H, *J* = 6.0, 8.4 Hz, H-4), 3.74 (dd, 1H, *J* = 2.8, 10.7 Hz, H-6); ^{13}C NMR (126 MHz, CD_2Cl_2) δ 144.78, 100.28, 77.13, 75.65, 74.74, 68.89, 54.23, 54.01, 53.80, 53.58, 53.37; FTIR (neat film) 3066, 2871, 2276, 2173, 2107, 2061, 1649, 1456, 1393, 1328, 1287, 1245, 1205, 1184, 1106, 962, 870, 839, 820, 743 cm^{-1}; HRMS (FAB) *m/z*: Calcd for $C_{27}H_7D_{21}O_4$ (M-H) 436.3229, found 436.3227.

3,4,6-Tri-O-benzyl-β-D-glucopyranosyl azide (4).[2] To the solution of 3,4,6-tri-*O*-benzyl-D-glucal (3) (50 mg, 0.12 mmol, 1 equiv), diphenyl sulfoxide (73 mg, 0.36 mmol, 3 equiv) and 2,4,6-tri-*tert*-butylpyridine (104 mg, 0.42 mmol, 3.5 equiv) in dichloromethane (3.3 mL) was added trifluoromethanesulfonic anhydride (30 μL, 0.18 mmol, 1.5 equiv) at –78 °C. The resulting solution was stirred at –78 °C for 30 min, and then at –40 °C for 1 h. Methyl alcohol (4.9 μL, 0.12 mmol, 1 equiv) and triethylamine (50 μL, 0.36 mmol, 3 equiv) were added sequentially at –40 °C. The solution was stirred at this temperature for 0.5 h, then at 0 °C for 0.5 h and finally at 23 °C for 1 h. The solvent was removed under reduce pressure at 0 °C, and the residue was then dissolved in dry CH_3CN (5 mL). NaN_3 (23 mg, 0.35 mmol, 3 equiv) and $LiClO_4$ (63 mg, 0.60 mmol, 5 equiv) were added sequentially to the reaction mixture at 0 °C, and the resulting suspension was stirred at 0 °C for 30 min, and then at 23 °C for 12 h. The reaction mixture was partitioned between dichloromethane (20 mL) and H_2O (20 mL) and the aqueous

layer was further extracted with dichloromethane (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and concentrated, and the residue was purified by flash column chromatography (17% ethyl acetate in hexane) to afford 3,4,6-tri-*O*-benzyl-β-D-glucopyranosyl azide (**4**) (44 mg, 77%) as white solid (from ethyl acetate-hexane), mp 63-64 °C; R_f = 0.60 (50% ethyl acetate in hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.28 (m, 13H, ArH), 7.18-7.17 (m, 2H, ArH), 4.89 (d, 1H, *J* = 11.4 Hz, benzylic-H), 4.84 (d, 1H, *J* = 11.2 Hz, benzylic-H), 4.82 (d, 1H, *J* = 10.7 Hz, benzylic-H), 4.63 (d, 1H, *J* = 12.2 Hz, benzylic-H), 4.56 (d, 1H, *J* = 10.7 Hz, benzylic-H), 4.55 (d, 1H, *J* = 12.2 Hz, benzylic-H), 4.53 (d, 1H, *J* = 8.6 Hz, H-1), 3.75 (dd, 1H, *J* = 2.6, 11.4 Hz, H-6), 3.73 (dd, 1H, *J* = 3.8, 11.2 Hz, H-6), 3.67 (dd, 1H, *J* = 9.0, 9.6 Hz, H-4), 3.55 (t, 1H, *J* = 9.0 Hz, H-3), 3.54 (ddd, 1H, *J* = 2.4, 3.9, 9.9 Hz, H-5), 3.45 (dt, 1H, 2.6, 8.8 Hz, H-2), 2.24 (d, 1H, *J* = 2.6 Hz, O*H*); MS (FAB) *m/z* (rel intensity, %) 498.2 (M+Na, 27), 472.3 (16), 177.1 (100); HRMS (FAB) *m/z*: Calcd for $C_{27}H_{29}N_3O_5Na$ (M+Na) 498.2007, found 498.2005.

3,4,6-Tri-*O*-benzyl-β-D-[2-^{18}O]-glucopyranosyl azide (4(^{18}O)). Prepared from 3,4,6-tri-*O*-benzyl-D-glucal (**3**, 41.4 mg, 0.100 mmol) as above, employing $Ph_2S^{18}O$ (*^{18}O* 96% incorp.), as the sulfoxide reagent. **4(^{18}O)** (37.6 mg, 79%): MS (FAB) *m/z* (rel intensity, %) 500.1 (M+Na, 100), 498.1 (8), 474.1 (43), 181.1 (88).

3,4,6-Tri-*O*-benzyl-α-D-mannopyranosyl azide (16). To the solution of DBTO (120 mg, 0.6 mmol, 5 equiv) and 2,4,6-tri-*tert*-butylpyridine (15 mg, 0.06 mmol, 0.5 equiv) in dichloromethane (2.5 mL) was added trifluoromethanesulfonic anhydride (40 μL, 0.24 mmol, 2 equiv) at –78 °C. The reaction was stirred at this temperature for 10 min, then at –45 °C for 1 h. The reaction mixture was re-cooled to –78 °C, and a solution of 3,4,6-tri-*O*-benzyl-D-glucal (**3**) (50 mg, 0.12 mmol, 1 equiv) in dichloromethane (2.5 mL) was added via cannula. The reaction

was stirred at –78 °C for 1 h before the sequential addition of methyl alcohol (4.9 μL, 0.12 mmol, 1 equiv) and $^{i}Pr_2NEt$ (122 μL, 0.71 mmol, 6 equiv). The solution was stirred at –78 °C for 10 min, then at –45 °C for 10 min, and finally at 0 °C for 1 h. The solvent was removed under reduce pressure at 0 °C, and the residue was dissolved in dry CH_3CN (5 mL). NaN_3 (24 mg, 0.36 mmol, 3 equiv) and $LiClO_4$ (65 mg, 0.61 mmol, 5 equiv) were added sequentially to the reaction mixture at 0 °C, and the resulting suspension was stirred at 0 °C for 30 min, and then at 23 °C for 18 h. The reaction was partitioned between dichloromethane (50 mL) and H_2O (20 mL), the aqueous layer was further extracted with dichloromethane (3 × 20 mL). The combined organic layers were washed with H_2O (3 × 15 mL), dried (Na_2SO_4) and concentrated, and the residue was purified by flash column chromatography (6% ethyl acetate in benzene then 11% ethyl acetate in benzene) to afford 3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl azide (**16**) (41 mg, 72%) as yellow oil and 3,4,6-tri-*O*-benzyl-β-D-glucopyranosyl azide (**4**) (8 mg, 13%). **16:** R_f = 0.73 (50% ethyl acetate in hexane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.28 (m, 13H, ArH), 7.20-7.17 (m, 2H, ArH), 5.46 (d, 1H, *J* = 2.0 Hz, H-1), 4.82 (d, 1H, *J* = 10.8 Hz, benzylic-H), 4.69 (d, 1H, *J* = 11.5 Hz, benzylic-H), 4.68 (d, 1H, *J* = 12.2 Hz, benzylic-H), 4.67 (d, 1H, *J* = 11.5 Hz, benzylic-H), 4.54 (d, 1H, *J* = 12.0 Hz, benzylic-H), 4.53 (d, 1H, *J* = 11.0 Hz, benzylic-H), 3.91-3.87 (m, 3H), 3.81-3.78 (m, 2H), 3.73 (dd, 1H, *J* = 1.7, 11.1 Hz), 2.61 (d, 1H, *J* = 2.1 Hz, O*H*); ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.07, 138.00, 137.51, 128.58, 128.36, 128.33, 128.09, 127.89, 127.87, 127.85, 127.73, 127.62, 89.27, 79.17, 75.13, 73.62, 73.49, 73.28, 72.27, 68.48, 68.24; FTIR (neat film) 3436, 3064, 3031, 2917, 2113, 1606, 1496, 1454, 1363, 1318, 1245, 1211, 1120, 1028, 932, 843, 798, 736, 698 cm^{-1}; MS (FAB) *m/z* (rel intensity, %) 498.2 (M+Na, 36), 472.2 (8), 177.0 (100); HRMS (FAB) *m/z*: Calcd for $C_{27}H_{29}N_3O_5Na$ (M+Na) 498.2007, found 498.2005.

3,4,6-Tri-*O*-benzyl-α-D-[2-^{18}O]-mannopyranosyl azide (16(^{18}O)). Prepared from 3,4,6-tri-*O*-benzyl-D-glucal (**3**, 42.2 mg, 0.1 mmol) as above, employing DBT^{18}O (*^{18}O* 95% incorp.), as the sulfoxide reagent. **16(^{18}O)** (35.5 mg, 73%): MS (FAB) *m/z* (rel intensity, %) 500.0 (M+Na, 78), 498.0 (8.5), 474.0 (74), 198.9 (90), 176.9 (100).

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[1] Sato, Y.; Kunieda, N.; Kinoshita, M. *Chem. Lett.* **1972**, 1023-1025.

[2] Gordon, D. M.; Danishefsky, S. J. *Carbohydr. Res.* **1990**, *206*, 361-366.