Two-Step Synthesis of Carbohydrates by Selective Aldol Reactions

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Supporting Information

General Information. Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego.[1] All solvents were purified according to the method of Grubbs.[2] Non-aqueous reagents were transferred under nitrogen via syringe or cannula. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator using an ice-water bath for volatile samples. Chromatographic purification of products was accomplished using forced-flow chromatography on ICN 60 32-64 mesh silica gel 63 according to the method of Still.[3] Thin-layer chromatography (TLC) was performed on EM Reagents 0.25 mm silica gel 60-F plates. Visualization of the developed chromatogram was performed by fluorescence quenching or by anisaldehyde, ceric ammonium molybdate, or $KMnO_4$ stain.

^1H and ^{13}C NMR spectra were recorded on a Mercury 300 (300 MHz and 75 MHz) or an Inova 500 (500 MHz and 125 MHz) as noted, and are internally referenced to residual protio solvent signals. Data for ^1H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration, coupling constant (Hz) and assignment. Data for ^{13}C NMR are reported in terms of chemical shift (δ ppm) for non-^{13}C labeled carbons or chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz) and assignment for ^{13}C labeled carbons. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in terms of frequency of absorption (cm^{-1}). Mass spectra were obtained from the California Institute of Technology Mass Spectral facility. Gas liquid chromatography (GLC) was performed on Hewlett-Packard 6850 and 6890 Series gas chromatographs equipped with a split-mode capillary

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[1]Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals;* 3rd ed., Pergamon Press, Oxford, 1988.
[2]Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518.

injection system and flame ionization detectors using a J&W Scientific DB-1701 (30 m x 0.25 mm) column as noted. High performance liquid chromatography (HPLC) was performed on Hewlett-Packard 1100 Series chromatographs using a Chiralcel OD-H column (25 cm) and OD-H guard (5 cm) as noted.

Preparation of Aldehyde Enolsilanes

(*Z*)-Acetic acid 2-(trimethylsilanyloxy)-vinyl ester. (7) Acetoxyacetaldehyde[4] (4.13 mL, 49.0 mmol) was added in a single portion to a room temperature solution of chlorotrimethylsilane (12.43 mL, 98.0 mmol), triethylamine (27.31 mL, 195.9 mmol), and acetonitrile (100 mL). In less than five minutes, the solution became a hot white suspension that turned into a rust-colored suspension within fifteen minutes. Volatiles were removed *in vacuo* and the residue was extracted with three 50 mL portions of anhydrous diethyl ether. Distillation of the ethereal extracts afforded the title compound (6.13 g, 35.2 mmol, b.p. 64 °C (10 mmHg), 9:1 *Z*:*E*) in 72% yield as a clear, colorless liquid. IR (film) 3112, 2962, 2903, 1757, 1682, 1368, 1254, 1223, 1124, 1059, 961.3, 850.1, 754.5, 658.1 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *Z* isomer: □ 6.56 (d, 1H, *J* = 3.3 Hz, CHOTMS); 5.77 (d, 1H, *J* = 3.3 Hz, CHOAc); 2.16 (s, 3H, $C(O)CH_3$); 0.23 (s, 9H, $Si(CH_3)_3$); *E* isomer: □ 7.11 (d, 1H, *J* = 10.5 Hz, CHOTMS); 6.66 (d, 1H, *J* = 10.5 Hz, CHOAc); 2.10 (s, 3H, $C(O)CH_3$); 0.20 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (75 MHz, $CDCl_3$) *Z* isomer: □ 168.2, 127.2, 121.2, 21.2, 0.0; HRMS (FAB+) exact mass calcd for $[M + H]^+$ ($C_7H_{15}O_3Si$) requires *m/z* 175.0791, found *m/z* 175.0788. The product ratios were determined by both ^1H NMR integrations and GLC analysis using a J&W Scientific DB-1701 column (50 ºC ramp 5 °C/min, 23 psi); *Z* isomer t_r = 10.46 min, *E* isomer t_r = 10.83 min.

(*Z*)-(2-Benzyloxy-vinyloxy)-trimethylsilane. (Table 1, Entry 1) Benzyloxyacetaldehyde (4.68 mL, 33.3 mmol) was added in a single portion to a room temperature solution of chlorotrimethylsilane (8.45 mL, 66.6 mmol), triethylamine (18.56 mL, 133 mmol), and acetonitrile (60 mL). In less than five minutes, the solution became a hot white suspension that turned into a rust-colored suspension within fifteen minutes. After stirring for 2 hours, volatiles were removed *in vacuo* and the residue was extracted with three 50 mL portions

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[3]Still, W. C.; Kahn, M.; Mitra, A. J. *J. Org. Chem.* **1978,** *43*, 2923.
[4] Brand, S.; Jones, M. F.; Rayner, C. M. *Tetrahedron Lett.* **1997**, *38*, 3595.

of anhydrous diethyl ether. Distillation of the ethereal extracts afforded the title compound (5.68 g, 25.5 mmol, b.p. 92 °C (0.08 mmHg), 12:1 *Z*:*E*) in 77% yield as a clear, colorless liquid. IR (film) 3034, 2959, 2901, 2872, 1667, 1497, 1455, 1397, 1362, 1298, 1252, 1129, 1026, 846.7, 734.0, 696.7 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) □ 7.33 (m, 5H, Ph-H); 5.49 (d, 1H, *J* = 3.3 Hz, CHOTMS); 5.44 (d, 1H, *J* = 3.3 Hz, CHOBn); 4.81 (s, 2H, $PhCH_2$); 0.21 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (75 MHz, $CDCl_3$) □ 137.7, 131.0, 128.6, 128.0, 127.7, 122.7, 74.1, –0.24; HRMS (FAB+) exact mass calcd for $[M + H]^+$ ($C_{12}H_{19}O_2Si$) requires *m*/*z* 223.1154, found *m*/*z* 223.1161. The product ratios were determined by ^1H NMR integration of the crude reaction mixture.

((*Z*)-[2-(Trimethylsilanyloxy)-vinyl]-carbamic acid *tert*-butyl ester)-trimethylsilyl-imidate. (Table 1, Entry 2) (2-Oxo-ethyl)-carbamic acid *tert*-butyl ester (3.0 g, 18.8 mmol) was added in a single portion as a solution in 10 mL of acetonitrile to a room temperature solution of chlorotrimethylsilane (4.78 mL, 37.7 mmol), triethylamine (10.51 mL, 75.4 mmol), and acetonitrile (30 mL). In less than five minutes, the solution became a hot white suspension that turned into a rust-colored suspension within fifteen minutes. After stirring for 3 hours, volatiles were removed *in vacuo* and the residue was extracted with three 50 mL portions of anhydrous diethyl ether. Distillation of the ethereal extracts afforded the title compound (3.67 g, 12.1 mmol, b.p. 66-68 °C, 0.25 mmHg, 13:1 *Z*:*E*) in 64% yield as a clear, colorless liquid. IR (film) 2977, 1709, 1689, 1482, 1392, 1367, 1313, 1251, 1170, 1086, 847.7, 784.3, 755.6 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) □ 5.97 (d, 1H, *J* = 2.7 Hz, CHOTMS); 5.25 (d, 1H, *J* = 2.7 Hz, CHN); 1.49 (s, 9H, $C(CH_3)_3$); 0.24 (s, 9H, $Si(CH_3)_3$); 0.20 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$) □ 157.1, 134.7, 111.4, 80.1, 28.6, 0.74, –0.25; HRMS (FAB+) exact mass calcd for $[M + H]^+$ ($C_{13}H_{29}NO_3Si_2$) requires *m*/*z* 303.1686, found *m*/*z* 303.1695. The product ratios were determined by ^1H NMR integration of the crude reaction mixture.

(*E*)-Thioacetic acid *S*-(4-acetylsulfanyl-but-2-enyl) ester. Potassium thioacetate (10.0 g, 87.6 mmol) was added to a room temperature solution of (*E*)-1,4-dibromo-2-butene (8.61 g, 35.0 mmol) in dimethylformamide (50 mL). After stirring for 3 hours, the suspension was treated with 500 mL 10% $NaHCO_3$, extracted with 250 mL ethyl acetate, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Purification of the residue by flash chromatography (4:1 hexanes:ether) afforded the title compound (5.49 g, 26.9 mmol) as a white crystalline solid

in 77% yield. IR (film) 3033, 2921, 1690, 1419, 1354, 1228, 1134, 960, 721.2, 683.4, 626.2 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 5.45 (m, 2H, CH=C); 3.30 (dd, 4H, J = 4.5, 1.8 Hz, CH_2); 2.14 (s, 6H, $C(O)CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) 194.4, 128.5, 30.9, 30.7; HRMS (EI+) exact mass calcd for $[M\bullet]^+$ ($C_8H_{12}O_2S_2$) requires *m/z* 204.0279, found *m/z* 204.0278.

Thioacetic acid *S*-(2-oxo-ethyl) ester. A stream of ozone was passed through a solution of (*E*)-thioacetic acid *S*-(4-acetylsulfanyl-but-2-enyl) ester (5.49 g, 26.9 mmol) in dichloromethane (125 mL) at –78 °C for 1 hour until a light blue color developed. Then, the reaction was treated with methyl sulfide (9.87 mL, 134 mmol) and allowed to warm slowly to room temperature and stirred until a KI/startch paper test was negative, indicating complete decomposition of the ozonide intermediate. Distillation of the reaction mixture afforded the title compound (2.30 g, 19.5 mmol, b.p. 78 °C, 10 mmHg) in 36% yield as a clear, colorless liquid. A significant amount of decomposition products were observed in the pot residue. IR (film) 2919, 2840, 2725, 1727, 1691, 1356, 1136, 1032, 951.2, 626.4 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 9.48 (t, 1H, J = 2.1 Hz, CH=O); 3.66 (d, 2H, J = 2.1 Hz, CH_2); 2.42 (s, 3H, $C(O)CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) 194.9, 194.0, 39.2, 30.6; HRMS (EI+) exact mass calcd for $[M\bullet]^+$ ($C_4H_6O_2S$) requires *m/z* 118.0089, found *m/z* 118.0086.

(*Z*)-Thioacetic acid *S*-[2-(trimethyl-silanyloxy)-vinyl] ester. (Table 1, Entry 3) Thioacetic acid *S*-(2-oxo-ethyl) ester (2.20 g, 18.6 mmol) was added in a single portion to a room temperature solution of chlorotrimethylsilane (4.72 mL, 37.2 mmol), triethylamine (10.4 mL, 74.5 mmol), and acetonitrile (40 mL). In less than five minutes, the solution became a hot white suspension that turned into a rust-colored suspension within fifteen minutes. After stirring for 1 hour, volatiles were removed *in vacuo* and the residue was extracted with three 50 mL portions of anhydrous diethyl ether. Distillation of the ethereal extracts afforded the title compound (2.40 g, 12.6 mmol, b.p. 66–68 °C, 3 mmHg, 3:1 *Z*:*E*) in 68% yield as a clear, colorless liquid. IR (film) 3076, 2960, 2901, 1700, 1624, 1419, 1353, 1255, 1227, 1183, 1125, 1083, 956.7, 891.8, 847.6, 754.6, 720.5, 619.3 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *Z* isomer: 6.50 (d, 1H, J = 5.1 Hz, CHOTMS); 5.67 (d, 1H, J = 5.1 Hz, CHSAc); 2.34 (s, 3H, $C(O)CH_3$); 0.20 (s, 9H, $Si(CH_3)_3$); *E* isomer: 6.53 (d, 1H, J = 12.0 Hz, CHOTMS); 5.59 (d, 1H, J = 12.0 Hz, CHSAc); 2.30 (s, 3H, $C(O)CH_3$); 0.22 (s, 9H, $Si(CH_3)_3$); ^{13}C NMR (75 MHz, $CDCl_3$) *Z* isomer 192.5, 140.7, 96.5,

30.8, –0.09; *E* isomer 196.3, 149.4, 97.0, 30.2, –0.04; HRMS (EI+) exact mass calcd for $[M\bullet]^+$ ($C_7H_{14}O_2SiS$) requires *m/z* 190.0484, found *m/z* 190.0480. Product ratios were determined by ^1H NMR integrations of the crude reaction mixture.

Preparation of ^{13}C–Labeled Sugar Precursors

Acetic acid 1,2-bis-^{13}C-2-hydroxy-ethyl ester. The title compound was prepared according to the method of Kusumoto *et al.*[5] Trimethylorthoacetate (2.98 mL, 23.4 mmol) was added to a room temperature stirring solution of $^{13}C_2$-ethylene glycol (1.00 g, 15.6 mmol), *p*-toulenesulfonic acid monohydrate (148 mg, 0.78 mmol) and dichloromethane (150 mL). After stirring for 6 minutes, deionized water (422 μL, 23.4 mmol) was added in a single portion. After an additional 6 minutes of stirring, volatiles were removed *in vacuo* and the residue was passed through a short plug of silica gel with 9:1 diethyl ether:hexanes as eluent to afford the title compound in quantitative yield (1.66 g, 15.6 mmol) as a clear, colorless liquid. IR (film) 3400, 2947, 2870, 1733, 1456, 1380, 1251, 1061, 1036, 950.7, 872.8, 608.9 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 4.20 (m, 2H, $J_{13C–1H}$ = 144.9 Hz, CH_2OAc); 3.82 (m, 2H, $J_{13C–1H}$ = 141.3 Hz, CH_2OH); 2.10 (s, 3H, CH_3); ^1H NMR (300 MHz, $CDCl_3$, ^{13}C decoupled) 4.21 (t, 2H, J = 4.2 Hz, CH_2OAc); 3.84 (m, 2H, CH_2OH); 2.11 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 171.6, 66.4 (d, $J_{13C–13C}$ = 40.1 Hz), 61.4 (d, $J_{13C–13C}$ = 40.1 Hz), 21.3; HRMS (EI+) exact mass calcd for $[M + H]^+$ ($^{13}C_2{}^{12}C_2H_9O_3$) requires *m/z* 107.0619, found *m/z* 107.0617.

Acetic acid 1,2-bis-^{13}C-2-oxo-ethyl ester. Acetic acid 1,2-bis-^{13}C-2-hydroxy-ethyl ester (1.66 g, 15.6 mmol) was added as a solution in 5 mL of dichloromethane to a room temperature stirring solution of Dess-Martin periodinane (8.30 g, 19.6 mmol) dissolved in dichloromethane (80 mL). After 3 hours, volatiles were removed *in vacuo* on a rotary evaporator while cooling the suspension in an ice-water bath. The residue was extracted with 3x50 mL of pentane, then concentrated *in vacuo* at 50-55 °C and 30 mmHg for 30 minutes to remove a portion of the excess acetic acid. ^1H NMR analysis of the pot residue (2.73 g) indicated a 1:2 ratio of the title compound (1.27 g, 12.2 mmol, 78% yield) to acetic acid. A small sample was purified by flash

chromatography (4:1 ethyl acetate:hexanes) for characterization purposes. IR (film) 2953, 1739, 1725, 1677, 1436, 1377, 1234, 1042 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 9.61 (dd, 1H, J_{13C-1H} = 179.1, 29.1 Hz, CHO); 4.67 (dd, 2H, J_{13C-1H} = 146.7, 3.9 Hz, CH_2OAc); 2.19 (s, 3H, CH_3); ^1H NMR (300 MHz, $CDCl_3$, ^{13}C decoupled) 9.59 (s, 1H, CHO); 4.66 (s, 2H, CH_2OAc); 2.18 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 195.7 (d, $J_{13C-13C}$ = 41.9 Hz), 170.6, 68.9 (d, $J_{13C-13C}$ = 41.9 Hz), 20.7; HRMS (EI+) exact mass calcd for $[M + H]^+$ ($^{13}C_2{}^{12}C_2H_7O_3$) requires *m/z* 105.0418, found *m/z* 105.0421.

(*Z*)-Acetic acid 1,2-bis-^{13}*C*-2-(trimethylsilanyloxy)-vinyl ester. The above described mixture of acetic acid and acetic acid 1,2-bis-^{13}*C*-2-oxo-ethyl ester (2.73 g, 12.2 mmol) was added as a solution in 3.0 mL acetonitrile in a single portion to a room temperature solution of chlorotrimethylsilane (6.19 mL, 48.8 mmol), triethylamine (10.2 mL, 73.2 mmol), and acetonitrile (22 mL). In less than five minutes, the solution became a hot white suspension that turned into a rust-colored suspension within fifteen minutes. After stirring for 2 hours, volatiles were removed *in vacuo* and the residue was extracted with three 25 mL portions of anhydrous diethyl ether. Distillation of the ethereal extracts afforded the title compound (1.38 g, 7.8 mmol, b.p. 67-69 °C, 10 mmHg, 7:1 *Z*:*E*) in 64% yield as a clear, colorless liquid. IR (film) 3102, 3032, 2962, 2904, 1756, 1628, 1420, 1375, 1254, 1223, 1168, 1110, 1050, 953.9, 850.1, 754.1, 652.7 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 6.55 (ddd, 1H, J_{13C-1H} = 175.8, 19.2, J_{1H-1H} = 3.9 Hz, CHOTMS); 5.77 (ddd, 1H, J_{13C-1H} = 179.4, 23.7, J_{1H-1H} = 3.9 Hz, CHOAc); 2.16 (s, 3H, CH_3); 0.22 (s, 9H, TMS); ^1H NMR (300 MHz, $CDCl_3$, ^{13}C decoupled) identical to (*Z*)-acetic acid 2-(trimethyl-silanyloxy)-vinyl ester (*vide supra*); ^{13}C NMR (75 MHz, $CDCl_3$) 168.4, 126.9 (d, $J_{13C-13C}$ = 92.2 Hz), 120.9 (d, $J_{13C-13C}$ = 92.3 Hz), 21.1, –0.08; HRMS (EI+) exact mass calcd for $[M + H]^+$ ($^{13}C_2{}^{12}C_5H_{14}O_3Si$) requires *m/z* 176.0779, found *m/z* 176.0785. The product ratios were determined by both ^1H NMR integrations and GLC analysis using a J&W Scientific DB-1701 column (50 ºC ramp 5 °C/min, 23 psi); *Z* isomer t_r = 10.46 min, *E* isomer t_r = 10.83 min.

1,2-bis-^{13}*C*-2-(Triisopropylsilanyloxy)-ethanol. The title compound was prepared according to the method of McDougal *et al.*[6] $^{13}C_2$-ethylene glycol (1.00 g, 15.6 mmol) was

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[5] Oikawa, M.; Wada, A.; Okazaki, F.; Kusumoto, S. *J. Org. Chem.* **1996**, *61*, 4469.
[6] McDougal, P. G.; Rico, S. G.; Oh, Y. -I.; Condon, B. D. *J. Org. Chem.* **1986**, *51*, 3388.

added dropwise to 60% sodium hydride in mineral oil (624 mg, 15.6 mmol) suspended in 30 mL of tetrahydrofuran. After 1 hour of vigorous stirring, chlorotriisopropylsilane (3.34 mL, 15.6 mmol) was added in a single portion and the solution was stirred for an additional 3.5 hours at room temperature. Then, the reaction was acidified with 250 mL saturated aqueous NH_4Cl, extracted with 250 mL ethyl acetate, washed with 100 mL 10% $NaHCO_3$, 100 mL brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The oily residue was purified by flash chromatography (9:1 hexanes:ethyl acetate) to afford the title compound as a clear, colorless oil (2.83g, 12.8 mmol, 82%). IR (film) 3369, 2943, 2892, 2866, 1464, 1384, 1367, 1249, 1103, 1035, 923.6, 882.4, 734.0, 680.1 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.80 (m, 2H, J_{13C-1H} = 138.9 Hz, CH_2OTIPS); 3.67 (m, 2H, J_{13C-1H} = 145.5 Hz, C**H$_2$**OH); 2.18 (m, 1H, OH); 1.07 (m, 21H, TIPS); ^1H NMR (300 MHz, $CDCl_3$, ^{13}C decoupled) δ 3.80 (t, 2H, J = 5.1 Hz, CH_2OTIPS); 3.66 (q, 2H, J = 4.8 Hz, CH_2OH); 2.19 (t, 1H, J = 6.0 Hz, OH); 1.08 (m, 21H, TIPS); ^{13}C NMR (75 MHz, $CDCl_3$) δ 64.6 (d, $J_{13C-13C}$ = 39.6 Hz), 64.0 (d, $J_{13C-13C}$ = 39.6 Hz), 18.3, 12.3; HRMS (EI+) exact mass calcd for $[M + H]^+$ ($^{13}C_2{}^{12}C_9H_{27}O_2Si$) requires *m/z* 221.1843, found *m/z* 221.1837.

1,2-bis-^{13}*C*-(Triisopropylsilanyloxy)-acetaldehyde. Oxallyl chloride (2.16 mL, 24.8 mmol) was added dropwise to –78 °C solution of methyl sulfoxide (3.52 mL, 49.5 mmol) and triethylamine (8.63 mL, 61.9 mmol) dissolved in dichloromethane (115 mL). After stirring for 5 minutes, 1,2-bis-^{13}*C*-2-(triisopropylsilanyloxy)-ethanol (2.73 g, 12.4 mmol) was added via cannula as a solution in 10 mL of dichloromethane (8 mL followed by 2 mL rinse). After 30 minutes, the stirring solution was allowed to warm to 0 °C over the course of 1 hour. Then, 75 mL of dichloromethane was added and the reaction mixture was washed with 100 mL saturated aqueous NH_4Cl, 100 mL 10% $NaHCO_3$, 100 mL brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The oily residue was purified by flash chromatography (9:1 hexanes:ethyl acetate) to afford the title compound as a clear, colorless oil (2.31g, 10.6 mmol, 86%). IR (film) 2944, 2892, 2867, 1701, 1464, 1117, 1064.5, 882.1, 788.0, 683.3 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.74 (ddt, 1H, J_{13C-1H} = 175.2, 24.6 Hz, J_{1H-1H} = 1.2 Hz, CHO); 4.25 (ddd, 2H, J_{13C-1H} = 141.3, 4.2 Hz, J_{1H-1H} = 1.2 Hz, CH_2OTIPS); 1.08 (m, 21H, TIPS); ^1H NMR (300 MHz, $CDCl_3$, ^{13}C decoupled) δ 9.75 (s, 1H, CHO); 4.27 (s, 2H, CH_2OTIPS); 1.10 (m, 21H, TIPS); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.1 (d, $J_{13C-13C}$ = 44.2 Hz), 70.0 (d, $J_{13C-13C}$ = 44.1 Hz),

18.2, 12.2; HRMS (EI+) exact mass calcd for $[M + H]^+$ ($^{13}C_2{}^{12}C_9H_{25}O_2Si$) requires *m/z* 219.1691, found *m/z* 219.1684.

(2*R*, 3*R*)-1,2,3,4-tetra-^{13}C-3-Hydroxy-2,4-bis-(triisopropylsilanyloxy)-butyraldehyde. D-Proline (38.2 mg, 0.33 mmol) was added to a room temperature solution of 1,2-bis-^{13}C-(triisopropylsilanyloxy)-acetaldehyde (1.45 g, 6.64 mmol) dissolved in methyl sulfoxide (13.3 mL). After 28 hours, the solution was diluted with 150 mL ethyl acetate, washed with 100 mL water, 100 mL brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Crude ^{1}H NMR analysis indicated complete conversion to a 4:1 mixture of *anti* to *syn* isomers. The oily residue was purified by flash chromatography (49:1 pentane:THF) to afford the title compound as a single diastereomer of a low melting solid (908 mg, 2.1 mmol) as well as a faster eluting mixture of isomers that was principally composed of the *syn* isomer (366 mg, 0.84 mmol) in a combined yield of 88%. IR (film) 3488, 2943, 2892, 2867, 1695, 1464, 1384, 1248, 1098, 1065, 882.4, 683.3 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) □ 9.67 (ddd, 1H, $J_{13C–1H}$ = 178.5, 21.9 Hz, $J_{1H–1H}$ = 1.8 Hz, CHO); 4.24 (m, 1H, C**H**CHO); 3.97 (m, 1H, C**H**OH); 3.87 (m, 2H, CH_2); 2.44 (m, 1H, OH); 1.09 (m, 42H, 2 TIPS); ^{1}H NMR (300 MHz, $CDCl_3$, ^{13}C decoupled) □ 9.68 (d, 1H, *J* = 6.6 Hz CHO); 4.25 (m, 1H, C**H**CHO); 3.97 (m, 1H, C**H**OH); 3.81 (m, 2H, CH_2); 2.44 (m, 1H, OH); 1.08 (m, 42H, 2 TIPS); ^{13}C NMR (75 MHz, $CDCl_3$) □ 202.3 (d, $J_{13C–13C}$ = 43.8 Hz), 79.2 (dd, $J_{13C–13C}$ = 43.8, 40.1 Hz), 74.6 (dd, $J_{13C–13C}$ = 42.3, 40.4 Hz), 63.0 (d, $J_{13C–13C}$ = 42.3 Hz), 18.3 (2C), 12.7, 12.2; HRMS (FAB+) exact mass calcd for $[M + H]^+$ ($^{13}C_4{}^{12}C_{18}H_{49}O_4Si_2$) requires *m/z* 437.3304, found *m/z* 437.3304. $[□]_D$ = 2.2 (c = 2.00, $CHCl_3$). The enantioselectivity of this sample was determined to be 95% ee by the method described for (*2S*, *3S*)-3-hydroxy-2,4-bis-(triisopropylsilanyloxy)-butyraldehyde.[7]

Aldol Reactions

2-*O*-Acetyl-4,6-bis-*O*-triisopropylsilyl-□,□-L-glucopyranose. (8) (2*S*, 3*S*)-3-Hydroxy-2,3-bis-triisopropylsilanoxy-propionaldehyde (200 mg, 0.46 mmol) was added as a solution in 2.3 mL of ethyl ether to a flame-dried flask charged with magnesium bromide diethyl etherate

[7] Northrup, A. B.; Mangion, I. K.; Hettche, F. *Angew. Chem. Int. Ed.* **2004**, *43*, 2152.

(358 mg, 1.39 mmol) and 2.3 mL of ethyl ether cooled to –20 °C. After stirring for 30 minutes at –20 °C, (*Z*)-acetic acid 2-(trimethyl-silanyloxy)-vinyl ester (169 μL, 0.92 mmol) was added. The suspension was stirred at –20 °C for 2 hours, then allowed to warm to +4 °C over the course of 4 hours. After stirring for an additional 24 hours at +4 °C, the reaction was acidified by the addition of 100 mL saturated aqueous NH_4Cl and extracted with ethyl acetate (2x50 mL). The combined organics were washed with 100 mL brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was taken up in 5 mL of 7:2:1 THF:water:trifluoroacetic acid at 0 °C and stirred for 30 minutes before being basified with 50 mL 10% $NaHCO_3$, extracted with 100 mL ethyl acetate, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Crude ^{1}H NMR analysis indicated complete conversion to a 10:1 mixture of glucose:mannose derived diastereomers as well as some minor acetal side-products. Flash chromatography (1:1 ether:hexanes) afforded the title compound as a clear, colorless oil that solidified slowly upon standing at room temperature under reduced pressure (182 mg, 0.34 mmol, stains blue/green in anisaldehyde, 2:1 α:β, 74%) as well as the slower eluting 2-*O*-acetyl-4,6-bis-*O*-triisopropylsilyl-α-L-mannopyranose product (12 mg, 0.02 mmol, stains red/rust brown in anisaldehyde, 5%) in 79% combined yield. IR (film) 3447, 2944, 2892, 2867, 1725, 1464, 1381, 1251, 1125, 1056, 882.8, 786.3, 681.6 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) α-isomer: δ 5.36 (dd, 1H, *J* = 4.0, 4.0 Hz, H1); 4.61 (m, 1H, H2); 3.96 (m, 1H, H3); 3.75 (m, 1H, H4); 3.87 (m, 1H, H5); 3.98 (m, 2H, H6); 2.31 (d, 1H, *J* = 5.0 Hz, C3 OH); 2.13 (s, 3H, C(O)CH_3); 1.16-1.00 (m, 42H, 6 $CH(CH_3)_2$); β-isomer: δ 4.66 (dd, 1H, *J* = 8.0, 8.0 Hz, H1); 4.61 (m, 1H, H2); 3.60 (ddd, 1H, *J* = 9.0, 9.0, 5.0 Hz, H3); 3.77 (m, 1H, H4); 3.35 (ddd, 1H, *J* = 7.5, 5.0, 2.0 Hz, H5); 3.87 (m, 2H, H6); 2.50 (d, 1H, *J* = 4.5 Hz, C3 OH); 2.14 (s, 3H, C(O)CH_3); 1.16-1.00 (m, 42H, 6 $CH(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) α-isomer: δ 171.3, 90.2 (C1), 74.5 (C2), 73.4 (C4), 72.5 (C3), 72.3 (C5), 63.5 (C6), 21.2, 18.6, 18.5, 18.2, 18.1, 13.3, 12.2; β-isomer: δ 172.3, 95.2 (C1), 78.5 (C5), 76.9 (C2), 76.1 (C3), 72.4 (C4), 63.2 (C6), 21.2, 18.6, 18.5, 18.2, 18.1, 13.3, 12.2; 500 MHz COSY and HMQC spectra support the above ^{1}H and ^{13}C NMR assignments; HRMS (FAB+) exact mass calcd for $[M+H]^+$ ($C_{26}H_{55}O_7Si_2$) requires *m/z* 535.3486, found *m/z* 535.3487; $[\alpha]_D$ = –30.5 (c = 2.00, $CHCl_3$, 2:1 α:β mixture).

Determination of the Relative Stereochemistry of 2-Acetoxy-4,6-bis-triisopropylsilanoxy-α,β-L-glucopyranose by Correlation to Glucose Pentaacetate.

Triethylamine (16 μL, 0.11 mmol), 4-dimethylaminopyridine (2.0 mg, 0.02 mmol), and acetic anhydride (8 μL, 0.08 mmol) were added to 2-*O*-acetyl-4,6-bis-*O*-triisopropylsilyl-α,β-L-glucopyranose (15.1 mg, 0.03 mmol) dissolved in dichloromethane (100 μL) at 0 °C and allowed to stir for 30 minutes before being moved to room temperature for 4 hours. The reaction was then acidified with 10 mL 1N HCl, extracted with 10 mL ethyl acetate, washed with 10 mL 10% $NaHCO_3$, 10 mL brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash chromatography (3:1 hexanes:ether) to afford a mixture of two diastereomeric triacetates (16 mg, 0.03 mmol) in nearly quantitative yield. The triacetates (16 mg, 0.03 mmol) were dissolved in THF (500 μL) along with tetrabutylammonium fluoride hydrate (27 mg, 0.10 mmol) and acetic acid (6 μL, 0.10 mmol) and heated to reflux for 3 hours. Then, triethylamine (100 μL, 0.72 mmol), 4-dimethylaminopyridine (2.0 mg, 0.02 mmol), and acetic anhydride (50 μL, 0.32 mmol) were added and the resulting suspension was stirred for an additional hour at reflux. Then, the suspension was cooled to room temperature, acidified with 10 mL 1N HCl, extracted with 10 mL ethyl acetate, washed with 10 mL 10% $NaHCO_3$, 10 mL brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was then purified by flash chromatography (1:1 ethyl acetate:hexanes) to afford a 2:1 mixture of pentaacetates in quantitative yield (10 mg, 0.03 mmol). A comparison of the ^1H and ^{13}C NMR spectra of the above generated pentaacetates to spectra recorded from commericially available (Aldrich Chemical Company) α-D-glucose pentaacetate and β-D-glucose pentaacetate showed that the major pentaacetate isomer was spectroscopically identical to β-D-glucose pentaacetate and the minor pentaacetate isomer was spectroscopically identical to α-D-glucose pentaacetate.

1,2,3,4,5,6-hexa-^{13}C-2-*O*-Acetyl-4,6-bis-*O*-triisopropylsilyl-α,β-D-glucopyranose. (11) Prepared according to the method above for 2-*O*-acetyl-4,6-bis-*O*-triisopropylsilyl-α,β-L-glucopyranose using (2*R*, 3*R*)-1,2,3,4-tetra-^{13}C-3-hydroxy-2,4-bis-(triisopropylsilanyloxy)-butyraldehyde (100 mg, 0.23 mmol), magnesium bromide diethyl etherate (177 mg, 0.69 mmol), (*Z*)-acetic acid 1,2-bis-^{13}*C*-2-(trimethylsilanyloxy)-vinyl ester (101 mg, 0.57 mmol) and 2.3 mL of ethyl ether. Crude ^1H and ^{13}C NMR analysis indicated complete conversion to a 8:1 mixture of glucose:mannose derived diastereomers as well as some minor acetal side-products. Flash chromatography (2:3 ether:hexanes + 1% triethylamine) afforded the title compound as a clear, colorless oil (83 mg, 0.15 mmol, stains blue/green in anisaldehyde, 2:1 α:β, 67%) as well as the

slower eluting 2-acetoxy-4,6-bis-triisopropylsilanoxy-α-D-mannopyranose product (4.2 mg, 0.01 mmol, stains red/rust brown in anisaldehyde, 3%) in 70% combined yield. IR (film) 3446, 2944, 2892, 2867, 1727, 1464, 1375, 1249, 1120, 1039, 883.1, 778.6, 681.5 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) α-isomer: δ 5.39 (m, 1H, $J_{13C–1H}$ = 171.5 Hz, H1); 4.64 (m, 1H, $J_{13C–1H}$ = 150.1 Hz, H2); 3.96 (m, 1H, H3); 3.75 (m, 1H, H4); 3.87 (m, 1H, H5); 3.98 (m, 2H, H6); 2.28 (m, 1H, C3 OH); 2.15 (s, 3H, $C(O)CH_3$); 1.23-1.04 (m, 42H, 6 $CH(CH_3)_2$); β-isomer: δ 4.66 (m, 1H, H1); 4.61 (m, 1H, H2); 3.60 (m, 1H, H3); 3.77 (m, 1H, H4); 3.35 (m, 1H, H5); 3.87 (m, 2H, H6); 2.42 (m, 1H, C3 OH); 2.16 (s, 3H, $C(O)CH_3$); 1.23-1.04 (m, 42H, 6 $CH(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) α-isomer: δ 171.2, 90.2 (d, $J_{13C-13C}$ = 46.1 Hz, C1), 74.5 (m, C2), 73.5 (m, C4), 72.5 (C3), 72.3 (C5), 63.3 (d, $J_{13C-13C}$ = 43.8 Hz, C6), 21.2, 18.6, 18.6, 18.2, 18.1, 13.3, 12.3; β-isomer: δ 172.2, 95.2 (d, $J_{13C-13C}$ = 44.8 Hz, C1), 78.6 (dd, $J_{13C-13C}$ = 42.9, 42.9 Hz, C5), 77.0 (dd, $J_{13C-13C}$ = 40.9, 38.5 Hz, C2), 76.0 (dd, $J_{13C-13C}$ = 38.5, 38.5 Hz, C3), 72.4 (m, C4), 63.0 (d, $J_{13C-13C}$ = 44.5 Hz, C6), 21.2, 18.6, 18.6, 18.2, 18.1, 13.3, 12.3; 500 MHz COSY and HMQC spectra support the above ^1H and ^{13}C NMR assignments; HRMS (FAB) exact mass calcd for $[M – OH]^-$ ($^{13}C_6{}^{12}C_{20}H_{53}O_6Si_2$) requires *m/z* 523.3582, found *m/z* 523.3588; $[\alpha]_D$ = 35.0 (c = 2.00, $CHCl_3$, 2:1 α:β mixture). ^1H NMR (500 MHz, $CDCl_3$, ^{13}C decoupled) was identical to that reported above for 2-*O*-acetyl-4,6-bis-*O*-triisopropylsilyl-α,β-L-glucopyranose. Additional confirmation of the glucose stereochemistry for these two anomeric products is the similarity in ^{13}C shifts to the unlabeled material above. The isotopic purity of >98% is estimated by the lack of any $^{13}C–^{13}C$ uncoupled resonances in the ^{13}C NMR spectrum and no observed $^{13}C–^1H$ uncoupled resonances in the ^1H NMR spectrum.

2-*O*-Acetyl-4,6-bis-*O*-triisopropylsilyl-α-L-mannopyranose. (9) (2*S,* 3*S*)-3-Hydroxy-2,3-bis-triisopropylsilanoxy-propionaldehyde (200 mg, 0.46 mmol) was added as a solution in 4.6 mL of dichloromethane to a flame-dried flask charged with magnesium bromide diethyl etherate (358 mg, 1.39 mmol) and 4.6 mL of dichloromethane cooled to –20 °C. After stirring for 30 minutes at –20 °C, (*Z*)-acetic acid 2-(trimethyl-silanyloxy)-vinyl ester (242 mg, 1.39 mmol) was added. The –20 °C suspension was stirred for 2 hours, then allowed to warm to +4 °C over the course of 4 hours. After stirring for an additional 18 hours at +4 °C, the reaction was acidified by the addition of 100 mL saturated aqueous NH_4Cl and extracted with ethyl acetate (2x50 mL). The combined organics were washed with 100 mL brine, dried over anhydrous

Na_2SO_4 and concentrated *in vacuo*. The residue was taken up in 5 mL of 7:2:1 THF:water:trifluoroacetic acid at 0 °C and stirred for 30 minutes before being basified with 50 mL 10% $NaHCO_3$, extracted with 100 mL ethyl acetate, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Crude ^{1}H NMR analysis indicated complete conversion to a >19:1 mixture of mannose:glucose derived diastereomers as well as some minor acetal side-products. Flash chromatography (2:3 ether:hexanes) afforded the title compound as a clear, colorless oil (207 mg, 0.39 mmol, stains red/rust brown in anisaldehyde, >19:1 □:□, 84%) as well as the faster eluting 2-*O*-acetyl-4,6-bis-*O*-triisopropylsilyl-□-L-glucoopyranose product (8.1 mg, 0.02 mmol, stains blue/green in anisaldehyde, 2:1 □:□, 3%) in 87% combined yield. IR (film) 3436, 2943, 2867, 1726, 1464, 1375, 1256, 1126, 1066, 883.2, 763.2, 681.6 cm^{-1}; While there is no detectable concentration effect on the ^{13}C NMR shifts, there is a significant concentration effect on the ^{1}H NMR shifts. Therefore, two ^{1}H NMR spectra have been provided: one at a high concentration (approx. 50 mg/mL), and one at a low concentration (approx. 2 mg/mL): ^{1}H NMR (500 MHz, $CDCl_3$) concentrated sample: □ 5.20 (m, 1H, H1); 5.09 (dd, 1H, *J* = 1.0, 1.0 Hz, H2); 4.17–3.91 (m, 4H, H3, H4, H6); 3.83 (m, 1H, H5); 3.61 (d, 1H, *J* = 1.0 Hz, C1 OH); 2.46 (d, 1H, *J* = 2.0 Hz, C3 OH); 2.10 (s, 3H, $C(O)CH_3$); 1.22-1.05 (m, 42H, 6 $CH(CH_3)_2$); dilute sample: □ 5.24 (dd, 1H, *J* = 4.0, 2.0 Hz, H1); 5.11 (dd, 1H, *J* = 2.5, 2.5 Hz, H2); 4.08 (m, 1H, H3); 4.11 (dd, 1H, *J* = 16.0, 8.0 Hz, H4); 3.79 (ddd, 1H, *J* = 8.0, 3.0, 3.0 Hz, H5); 3.99 (m, 2H, H6); 2.63 (d, 1H, *J* = 3.5 Hz, C1 OH); 2.11 (s, 3H, $C(O)CH_3$); 2.01 (d, 1H, *J* = 6.5 Hz, C3 OH); 1.27-1.09 (m, 42H, 6 $CH(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) □ 171.3, 92.1, 74.7, 73.6, 70.8, 69.9, 63.3, 21.2, 18.5, 18.5, 18.2, 18.1, 13.2, 12.3; 500 MHz COSY spectra support the above ^{1}H NMR assignments; HRMS (FAB) exact mass calcd for $[M - H]^-$ ($C_{26}H_{53}O_7Si_2$) requires *m/z* 533.3330, found *m/z* 533.3319; $[□]_D = -17.3$ (c = 2.00, $CHCl_3$).

Determination of the Relative and Absolute Stereochemistry of 2-*O*-Acetyl-4,6-bis-*O*-triisopropylsilyl-□-L-mannopyranose by Correlation to □-L-Mannose Pentaacetate.

Triethylamine (20 μL, 0.14 mmol), 4-dimethylaminopyridine (1.0 mg, 0.01 mmol), and acetic anhydride (10 μL, 0.11 mmol) were added to 2-*O*-acetyl-4,6-bis-*O*-triisopropylsilyl-□-L-mannopyranose (19.5 mg, 0.036 mmol) dissolved in dichloromethane (360 μL) at 0 °C and allowed to stir for 30 minutes before being moved to room temperature for 3 hours. The reaction was then acidified with 10 mL 1N HCl, extracted with 10 mL ethyl acetate, washed with 10 mL

10% $NaHCO_3$, 10 mL brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The crude triacetate (23 mg, 0.04 mmol) was dissolved in THF (500 μL) along with tetrabutylammonium fluoride hydrate (39 mg, 0.15 mmol) and acetic acid (8.5 μL, 0.15 mmol) and heated to reflux for 3 hours. Then, triethylamine (100 μL, 0.72 mmol), 4-dimethylaminopyridine (2.0 mg, 0.02 mmol), and acetic anhydride (50 μL, 0.32 mmol) were added and the suspension was stirred for an additional hour at reflux. The suspension was then cooled to room temperature, acidified with 10 mL 1N HCl, extracted with 10 mL ethyl acetate, washed with 10 mL 10% $NaHCO_3$, 10 mL brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was then purified by flash chromatography (1:1 ethyl acetate:hexanes) to afford a single pentaacetate in quantitative yield (13 mg, 0.04 mmol). A comparison of the ^{1}H and ^{13}C NMR spectra of the above generated pentaacetate to an authentic sample of β-D-mannose pentaacetate (generated by the method of Bonner[8]) showed the two compounds to be spectroscopically identical. The optical rotation of the correlated sample $[\alpha]_D$ = –54.0 (c = 1.00, $CHCl_3$) is opposite in sign and of similar magnitude to the reported value[9] for β-D-mannose pentaacetate $[\alpha]_D$ = 56.8 (c = 1.00, $CHCl_3$). The correlated sample, therefore, posses the L absolute stereochemistry.

1,2,3,4,5,6-hexa-^{13}C-2-*O*-Acetyl-4,6-bis-*O*-triisopropylsilyl-α-D-mannopyranose. (12) Prepared according to the method above for 2-*O*-acetyl-4,6-bis-*O*-triisopropylsilyl-α-L-mannopyranose using (2*R*, 3*R*)-1,2,3,4-tetra-^{13}C-3-hydroxy-2,4-bis-(triisopropylsilanyloxy)-butyraldehyde (250 mg, 0.57 mmol), magnesium bromide diethyl etherate (443 mg, 1.72 mmol), (*Z*)-acetic acid 1,2-bis-^{13}*C*-2-(trimethylsilanyloxy)-vinyl ester (303 mg, 1.72 mmol) and dichloromethane (11.4 mL). Crude ^{1}H and ^{13}C NMR analysis indicated complete conversion to a >19:1 mixture of mannose:glucose derived diastereomers as well as some minor acetal side-products. Flash chromatography (2:3 ether:hexanes) afforded the title compound as a clear, colorless oil (221 mg, 0.41 mmol, stains red/rust brown in anisaldehyde, >19:1 α:β, 71%). IR (film) 3445, 2944, 2893, 2867, 1728, 1464, 1374, 1253, 1107, 1060, 883.2, 747.7, 681.1 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) dilute sample: δ 5.22 (m, 1H, J_{13C-1H} = 171.0 Hz, H1); 5.10 (m, 1H,

[8] Bonner *J.Am.Chem.Soc*. **1958**, *80*, 3372.
[9] Bonner *J.Am.Chem.Soc*. **1958**, *80*, 3372.

$J_{13C–1H}$ = 153.0 Hz, H2); 4.23–3.56 (m, 5H, H3, H4, H5, H6); 2.91 (m, 1H, C1 OH); 2.11 (s, 3H, C(O)CH_3); 2.02 (m, 1H, C3 OH); 1.27-1.09 (m, 42H, 6 $CH(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) □ 171.2, 92.2 (d, $J_{13C-13C}$ = 47.1 Hz), 74.8 (dd, $J_{13C-13C}$ = 41.8, 41.8 Hz), 73.4 (dd, $J_{13C-13C}$ = 47.1, 36.5 Hz), 70.9 (dd, $J_{13C-13C}$ = 39.5, 39.5 Hz), 69.8 (dd, $J_{13C-13C}$ = 40.3, 40.3 Hz), 63.1 (d, $J_{13C-13C}$ = 44.1 Hz, C6), 21.1, 18.5, 18.5, 18.2, 18.1, 13.2, 12.3; HRMS (FAB+) exact mass calcd for $[M+H]^+$ ($^{13}C_6{}^{12}C_{20}H_{55}O_7Si_2$) requires *m/z* 541.3688, found *m/z* 541.3669; $[□]_D$ = 16.2 (c = 2.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$, ^{13}C decoupled) was identical to that reported above for a dilute sample of 2-*O*-acetyl-4,6-bis-*O*-triisopropylsilyl-□-L-mannopyranose. Additional confirmation of the mannose stereochemistry is the similarity in ^{13}C shifts to the unlabeled material above. The isotopic purity of >98% is estimated by the lack of any ^{13}C–^{13}C uncoupled resonances in the ^{13}C NMR spectrum and no observed ^{13}C–^{1}H uncoupled resonances in the ^{1}H NMR spectrum.

2-*O*-Acetyl-4,6-bis-*O*-triisopropylsilyl-□,□-L-allopyranose. (10) Titanium (IV) chloride (125 *μ*L, 1.13 mmol) was added dropwise to a stirring –78 °C solution of (2*S,* 3*S*)-3-hydroxy-2,3-bis-triisopropylsilanoxy-propionaldehyde (200 mg, 0.46 mmol), (*Z*)-acetic acid 2-(trimethyl-silanyloxy)-vinyl ester (241 mg, 1.39 mmol) and dichloromethane (9.2 mL). The resulting orange-red solution was stirred at –78 °C for 10 hours, then allowed to warm gradually over 3 hours to –40 °C. After stirring for an additional 4 hours at –40 °C, the reaction was acidified by the addition of 100 mL saturated aqueous NH_4Cl and extracted with ethyl acetate (2x50 mL). The combined organics were washed with 100 mL brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Crude ^{1}H NMR analysis indicated complete conversion to a >19:1 mixture of allose:mannose derived diastereomers as well as some minor acetal side-products. Flash chromatography (2:3 ether:hexanes) afforded the title compound as a clear, colorless oil (230 mg, 0.43 mmol, stains light green in anisaldehyde, 2:1 □:□, 93%) as well as the slower eluting 2-*O*-acetyl-4,6-bis-*O*-triisopropylsilyl-□-L-mannopyranose product (8 mg, 0.01 mmol, stains red/rust brown in anisaldehyde, 3%) in 96% combined yield. IR (film) 3406, 2944, 2867, 1742, 1464, 1374, 1236, 1050, 1014, 883.4, 681.6 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) □-isomer: □ 5.27 (d, 1H, *J* = 10.5 Hz, C1 OH); 5.16 (dd, 1H, *J* = 10.5, 3.5 Hz, H1); 4.68 (dd, 1H, *J* = 3.5, 3.0 Hz, H2); 4.32 (m, 1H, H3); 4.13 (dd, 1H, *J* = 9.5, 3.0 Hz, H4); 3.79 (ddd, 1H, 9.5, 2.5, 2.5 Hz, H5); 3.98 (m, 2H, H6); 3.09 (s, 1H, C3 OH); 2.19 (s, 3H, C(O)CH_3); 1.15-1.05 (m, 42H, 6

$CH(CH_3)_2$); β-isomer: δ 5.11 (dd, 1H, *J* = 8.5, 8.5 Hz, H1); 4.63 (dd, 1H, *J* = 8.0, 2.0 Hz, H2); 4.21 (apparent t, 1H, *J* = 3 Hz, H3); 4.02 (dd, 1H, *J* = 6.5, 3.0 Hz, H4); 3.72 (ddd, 1H, *J* = 9.0, 4.5, 2.0 Hz, H5); 3.87 (dd, 1H, *J* = 11.5, 5.0 Hz, one of H6); 3.97 (dd, 1H, *J* = 11.5, 3.0 Hz, one of H6); 3.23 (s, 1H, C1 OH); 2.57 (s, 1H, C3 OH); 2.18 (s, 3H, $C(O)CH_3$); 1.15-1.05 (m, 42H, 6 $CH(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) β-isomer: δ 170.5, 91.6 (C1), 72.0 (C3), 69.4 (C2), 68.1 (C5), 67.3 (C4), 62.4 (C6), 21.2, 18.3, 18.3, 18.2, 18.1, 12.8, 12.3; α-isomer: δ 171.4, 92.6 (C1), 75.4 (C5), 73.7 (C2), 70.7 (C3), 68.6 (C4), 63.1 (C6), 21.4, 18.3, 18.3, 18.2, 18.1, 12.8, 12.3; 500 MHz COSY and HMQC spectra support the above ^{1}H and ^{13}C NMR assignments; HRMS (FAB+) exact mass calcd for $[M+H]^+$ ($C_{26}H_{55}O_7Si_2$) requires *m/z* 535.3486, found *m/z* 535.3484; $[\alpha]_D = -26.6$ (c = 2.00, $CHCl_3$, 3.6:1 β:α mixture).

Determination of the Relative and Absolute Stereochemistry of 2-*O*-Acetyl-4,6-bis-*O*-triisopropylsilyl-α,β-L-allopyranose by Correlation to Allose Pentaacetate.

Triethylamine (34 μL, 0.24 mmol), 4-dimethylaminopyridine (1.0 mg, 0.01 mmol), and acetic anhydride (17 μL, 0.18 mmol) were added to 2-*O*-acetyl-4,6-bis-*O*-triisopropylsilyl-α,β-L-allopyranose (15.1 mg, 0.03 mmol, 4:1 β:α) dissolved in dichloromethane (1.0 mL) at 0 °C. After being allowed to stir for 1 hour at 0 °C, the solution was warmed to room temperature over the course of 1 hour. Then, the solution was heated to reflux for 5 hours with the addition of an additional 34 μL of triethylamine and 17 μL of acetic anhydride. The reaction was then acidified with 10 mL 1N HCl, extracted with 10 mL ethyl acetate, washed with 10 mL 10% $NaHCO_3$, 10 mL brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash chromatography (7:3 hexanes:ether) to afford the faster eluting α-anomer (7.7 mg, 0.01 mmol, 21%) as well as the slower eluting β-anomer (25 mg, 0.04 mmol, 67%) and an additional mixed fraction (4.8 mg, 0.01 mmol, 13%). The isolated triacetates were separately dissolved in THF (500 μL) along with tetrabutylammonium fluoride hydrate (4 equiv.) and acetic acid (4 equiv.) and heated to reflux for 3 hours. Then, triethylamine (100 μL, 0.72 mmol), 4-dimethylaminopyridine (2.0 mg, 0.02 mmol), and acetic anhydride (50 μL, 0.32 mmol) were added and the suspension was stirred for an additional hour at reflux. Then, the suspension was cooled to room temperature, acidified with 10 mL 1N HCl, extracted with 10 mL ethyl acetate, washed with 10 mL 10% $NaHCO_3$, 10 mL brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residues were then purified by flash chromatography (2:3 ethyl

acetate:hexanes) to afford 15.2 mg of the α-pentaacetate (96%, $[\alpha]_D$ = –2.6 (c = 1.00, $CHCl_3$)) and 3.6 mg of the β-pentaacetate (82%, $[\alpha]_D$ = 15.0 (c = 0.36, $CHCl_3$)). A comparison of the ^1H and ^{13}C NMR spectra of the above generated pentaacetates to spectra recorded from authentic samples of α-D-allose pentaacetate and β-D-allose pentaacetate prepared by the methods of Sims *et al.*[10] and Maurer *et al.*,[11] respectively, showed that the α-pentaacetate isomer was spectroscopically identical to α-D-allose pentaacetate and the β-pentaacetate isomer was spectroscopically identical to β-D-allose pentaacetate. Both generated pentaacetate isomers have optical rotations of opposite sign and similar magnitude to that reported in the literature, confirming the L-absolute stereochemistry for each anomer: α-D-allose pentaacetate lit.[12] $[\alpha]_D$ = 3.0 (c = 0.70, $CHCl_3$); β-D-allose pentaacetate lit.[13] $[\alpha]_D$ = –14.8 (c = 1.00, $CHCl_3$)

1,2,3,4,5,6-hexa-^{13}C-2-*O*-Acetyl-4,6-bis-*O*-triisopropylsilyl-D-allopyranose. (13) Prepared according to the method above for 2-*O*-acetyl-4,6-bis-*O*-triisopropylsilyl-L-allopyranose using (2*R*, 3*R*)-1,2,3,4-tetra-^{13}C-3-hydroxy-2,4-bis-(triisopropylsilanyloxy)-butyraldehyde (250 mg, 0.57 mmol), titanium (IV) chloride (157 μL, 1.43 mmol), (*Z*)-acetic acid 1,2-bis-^{13}*C*-2-(trimethylsilanyloxy)-vinyl ester (303 mg, 1.72 mmol) and 11.4 mL of dichloromethane. Crude ^1H and ^{13}C NMR analysis indicated complete conversion to a >19:1 mixture of allose:mannose derived diastereomers as well as some minor acetal side-products. Flash chromatography (2:3 ether:hexanes) afforded the title compound as a clear, colorless oil (269 mg, 0.50 mmol, stains light green in anisaldehyde, 2:1 α:β, 87%). IR (film) 3429, 2944, 2893, 2868, 1645, 1464, 1372, 1240, 1118, 1040, 883.2, 682.0 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) α-isomer: δ 5.27 (m, 1H, C1 OH); 5.16 (m, 1H, H1); 4.68 (m, 1H, H2); 4.32 (m, 1H, H3); 4.13 (m, 1H, H4); 3.79 (m, 1H, H5); 3.98 (m, 2H, H6); 3.10 (s, 1H, C3 OH); 2.18 (s, 3H, $C(O)CH_3$); 1.14-1.06 (m, 42H, 6 $CH(CH_3)_2$); β-isomer: δ 5.11 (m, 1H, H1); 4.63 (m, 1H, H2); 4.21 (m, 1H, H3); 4.02 (m, 1H, H4); 3.72 (m, 1H, H5); 3.87 (m, 1H, one of H6); 3.97 (m, 1H, one of H6); 3.23 (m, 1H, C1 OH); 2.56 (s, 1H, C3 OH); 2.17 (s, 3H, $C(O)CH_3$); 1.14-1.06 (m, 42H, 6 $CH(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) α-isomer: δ 170.5, 91.6 (d, $J_{13C\text{-}13C}$ = 44.1 Hz, C1), 72.0 (dd, $J_{13C\text{-}13C}$ = 35.6, 35.6 Hz, C3), 69.4 (dd, $J_{13C\text{-}13C}$ = 44.1, 39.5 Hz, C2), 68.1 (m, C5), 67.3 (m,

[10] Furneaux, R. H.; Rendle, P. M.; Sims, I. M. *J. Chem. Soc. Perkin Trans.1* **2000**, *11*, 2011.
[11] Weinges, K.; Haremsa, S.; Maurer, W. *Carb. Res.* **1987**, *164*, 453.
[12] Jensen, S. R.; Mikkelsen, C. B.; Nielsen, B. J. *Phytochemistry* **1981**, *20*, 71.

C4), 62.4 (d, $J_{13C\text{-}13C}$ = 41.8 Hz, C6), 21.2, 18.3, 18.3, 18.2, 18.1, 12.8, 12.3; β-isomer: δ 171.4, 92.6 (d, $J_{13C\text{-}13C}$ = 47.1 Hz, C1), 75.4 (dd, $J_{13C\text{-}13C}$ = 44.0, 44.0 Hz, C5), 73.7 (dd, $J_{13C\text{-}13C}$ = 47.1, 39.6 Hz, C2), 70.7 (dd, $J_{13C\text{-}13C}$ = 38.0, 38.0 Hz, C3), 68.6 (dd, $J_{13C\text{-}13C}$ = 43.4, 37.3 Hz, C4), 63.1 (d, $J_{13C\text{-}13C}$ = 44.9 Hz, C6), 21.3, 18.3, 18.3, 18.2, 18.1, 12.8, 12.3; HRMS (EI+) exact mass calcd for $[M^{\bullet+} - OH]^+$ ($^{13}C_6{}^{12}C_{20}H_{53}O_6Si_2$) requires *m/z* 523.3582, found *m/z* 523.3592; $[\alpha]_D$ = 16.8 (c = 2.00, $CHCl_3$, 2:1 α:β mixture). ^{1}H NMR (500 MHz, $CDCl_3$, ^{13}C decoupled) was identical to that reported above for 2-*O*-acetyl-4,6-bis-*O*-triisopropylsilyl-L-allopyranose. Additional confirmation of the allose stereochemistry for these two anomeric products is the similarity in ^{13}C shifts to the unlabeled material above. The isotopic purity of >98% is estimated by the lack of any ^{13}C–^{13}C uncoupled resonances in the ^{13}C NMR spectrum and no observed ^{13}C–^{1}H uncoupled resonances in the ^{1}H NMR spectrum.

2-*O*-Benzyl-4,6-bis-*O*-triisopropylsilyl-α-L-allopyranose. (14) In an inert atmosphere glove-box, a 25 mL flame-dried flask was charged with titanium (IV) chloride tetrahydrofuran complex (1:2) (386 mg, 1.16 mmol) and a magnetic stirbar. After being removed from the glove-box and placed under an argon atmosphere, 4.6 mL of dichloromethane was added and the solution was cooled to –78 °C. Then, (*Z*)-acetic acid 2-(trimethyl-silanyloxy)-vinyl ester (308 mg, 1.39 mmol) was added dropwise followed by a solution of (2*S,* 3*S*)-3-hydroxy-2,3-bis-triisopropylsilanoxy-propionaldehyde (200 mg, 0.46 mmol) in 4.6 mL of dichloromethane. The resulting blood-red solution was stirred at –78 °C for 1 hour before being allowed to gradually warm to –30 °C over the course of 3 hours. The reaction was then acidified by the addition of 100 mL saturated aqueous NH_4Cl, extracted with ethyl acetate (3x50 mL), washed with 100 mL 10% $NaHCO_3$, 100 mL brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Crude ^{1}H NMR analysis indicated complete conversion to a >19:1 mixture of allose:mannose derived diastereomers as well as some minor acetal side-products. Flash chromatography (3:7 ether:hexanes + 1% triethylamine) afforded the title compound as a clear, colorless oil (225 mg, 0.39 mmol, stains light green in anisaldehyde, 8:1 α:β, 83%). IR (film) 3293, 2943, 2866, 1464, 1388, 1248, 1138, 1089, 1068, 1016, 883.3, 680.5 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (m, 5H, Ar-H); 5.31 (br s, 1H, C1 OH); 5.21 (s, 1H, H1); 4.79 (d, 1H, *J* = 12.0 Hz, one of CH_2Ar); 4.63 (d, 1H, *J* = 12.0 Hz, one of CH_2Ar); 3.34 (dd, 1H, *J* = 3.5, 3.5 Hz, H2); 4.27 (m, 1H, C3);

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[13] Zissis; Richtmyer *J.Org.Chem.* **1961**, *26*, 5244.

3.97 (m, 1H, H4); 3.80 (ddd, 1H, *J* = 9.0, 2.0, 2.0 Hz, H5); 3.97 (m, 2H, H6); 2.98 (s, 1H, C3 OH); 1.14-1.03 (m, 42H, 6 $CH(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) □ 137.8, 128.7, 128.3, 128.2, 92.0, 74.1, 72.3, 71.2, 68.2, 67.7, 62.7, 18.3, 18.3, 18.2, 18.1, 12.9, 12.4; 500 MHz COSY spectra support the above ^1H NMR assignments; HRMS (FAB+) exact mass calcd for $[M+H]^+$ ($C_{31}H_{59}O_6Si_2$) requires *m/z* 583.3850, found *m/z* 583.3834; $[□]_D$ = –31.2 (c = 2.00, $CHCl_3$, 8:1 □:□ mixture).

Determination of the Relative Stereochemistry of 2-*O*-Benzyl-4,6-bis-*O*-triisopropylsilyl-□-L-allopyranose by Correlation to Allose Pentaacetate.

Triethylamine (10 equiv.), 4-dimethylaminopyridine (0.1 equiv.), and acetic anhydride (5 equiv.) were added to 2-*O*-benzyl-4,6-bis-*O*-triisopropylsilyl-□-L-allopyranose dissolved in dichloromethane at 0 °C and allowed to stir for 30 minutes before being moved to room temperature for 1 hour. Then, the solution was heated to reflux for 5 hours. The reaction was then acidified with 10 mL 1N HCl, extracted with 10 mL ethyl acetate, washed with 10 mL 10% $NaHCO_3$, 10 mL brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The crude diacetate was subjected to hydrogenolysis (50 psi H_2, 1:1 THF:EtOAc, 5 mg 10% Pd/C), followed by treatment with THF (500 μL) along with tetrabutylammonium fluoride hydrate (4 equiv.) and acetic acid (4 equiv.) and heated to reflux for 3 hours. Then, triethylamine (100 μL, 0.72 mmol), 4-dimethylaminopyridine (2.0 mg, 0.02 mmol), and acetic anhydride (50 μL, 0.32 mmol) were added and stirred for an additional hour at reflux. Then, the solution was cooled to room temperature, acidified with 10 mL 1N HCl, extracted with 10 mL ethyl acetate, washed with 10 mL 10% $NaHCO_3$, 10 mL brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was then purified by flash chromatography (2:3 ethyl acetate:hexanes). A comparison of the ^1H and ^{13}C NMR spectra of the above generated pentaacetate to spectra recorded from an authentic samples of □-D-allose pentaacetate prepared by the methods of Sims *et al.*[14] showed that the □-pentaacetate isomer was spectroscopically identical to □-D-allose pentaacetate.

2-*tert*-Butylcarbamoyl-2-deoxy-4,6-bis-*O*-triisopropylsilyl-α,β-L-mannopyranose.

(15) Titanium (IV) chloride (38 μL, 0.35 mmol) was added dropwise to a stirring –78 °C solution of (2*S,* 3*S*)-3-hydroxy-2,3-bis-triisopropylsilanoxy-propionaldehyde (50 mg, 0.12 mmol), ((*Z*)-[2-(trimethylsilanyloxy)-vinyl]-carbamic acid *tert*-butyl ester)-trimethylsilyl-imidate (175 mg, 0.58 mmol) and dichloromethane (2.3 mL). The resulting blood red solution was stirred at –78 °C for 5 hours, then allowed to warm gradually over 5 hours to –40 °C. After stirring for an additional 48 hours at –40 °C, the reaction was acidified by the addition of 100 mL saturated aqueous NH_4Cl, extracted with ethyl acetate (3x50 mL), washed with 100 mL 10% $NaHCO_3$, 100 mL brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Crude ^1H and ^{13}C NMR analysis indicated complete conversion to a 10:1 mixture of mannose:allose derived diastereomers as well as some minor acetal side-products. Flash chromatography (1:3 ether:hexanes) afforded the title compound as a clear, colorless oil (51 mg, 0.09 mmol, 2:1 α:β, 74%). IR (film) 3436, 2943, 2893, 2867, 1699, 1510, 1464, 1368, 1248, 1151, 1122, 1066, 883.0, 763.3, 680.9 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.92 (d, 1H, *J* = 9.0 Hz, OH); 7.59 (br s, 1H, NH); 5.13 (d, 1H, *J* = 3.0 Hz, H1); 4.95 (m, 1H, H3); 3.95 (m, 1H, H2); 4.10 (m, 1H, H4); 3.85 (m, 1H, H5); 3.96 (m, 2H, H6); 1.47 (d, 1H, *J* = 3.0 Hz, C3 OH); 1.45 (s, 9H, $C(CH_3)_3$); 1.22-1.06 (m, 42H, 6 $CH(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.1, 94.0, 80.5, 75.5, 71.2, 70.0 63.5, 54.5, 28.5, 18.5, 18.5, 18.2, 18.1, 13.0, 12.2; 500 MHz COSY spectra support the above ^1H NMR assignments; HRMS (EI+) exact mass calcd for $[M+H]^+$ ($C_{29}H_{62}NO_7Si_2$) requires *m/z* 592.4065, found *m/z* 592.4064; $[\alpha]_D$ = –27.1 (c = 2.00, $CHCl_3$, 2:1 α:β mixture).

Determination of the Relative and Stereochemistry of 2-*tert*-Butylcarbamato-2-deoxy-4,6-bis-*O*-triisopropylsilyl-α,β-L-mannopyranose by Correlation to 2-Acetamido-2-dexoy-1,3,4,6-tetra-*O*-acetyl-β-mannopyranose.

Triethylamine (81 μL, 0.58 mmol), 4-dimethylaminopyridine (1.4 mg, 0.01 mmol), and acetic anhydride (28 μL, 0.29 mmol) were added to a solution of 2-*tert*-butylcarbamato-2-deoxy-4,6-bis-*O*-triisopropylsilyl-α,β-L-mannopyranose (34.6 mg, 0.058 mmol) in dichloromethane (300 μL) and allowed to stir for 10 hours. The reaction was then acidified with 10 mL 1N HCl, extracted with 10 mL ethyl acetate, washed with 10 mL 10% $NaHCO_3$, 10 mL brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to afford 40 mg (3:1 α:β). The crude

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[14] Furneaux, R. H.; Rendle, P. M.; Sims, I. M. *J. Chem. Soc. Perkin Trans.1* **2000**, *11*, 2011.

diacetate was subjected to tetrabutylammonium fluoride hydrate (62 mg, 0.24 mmol) and acetic acid (13.5 μL, 0.24 mmol) in THF (120 μL) at reflux for 4 hours. Then, triethylamine (100 μL, 0.72 mmol), 4-dimethylaminopyridine (2.0 mg, 0.02 mmol), and acetic anhydride (50 μL, 0.32 mmol) were added and stirred for an additional hour at reflux. Then, the solution was cooled to room temperature, acidified with 10 mL 1N HCl, extracted with 10 mL ethyl acetate, washed with 10 mL 10% $NaHCO_3$, 10 mL brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The crude tetraacetate was then dissolved in 5:1 dichloromethane:trifluoroacetic acid (1.0 mL) and stirred for 5 hours at room temperature. Then, the reaction was basified with 10 mL $NaHCO_3$, extracted with ethyl acetate (3x10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Then, the residue was dissolved in 200 μL of dichloromethane and triethylamine (100 μL, 0.72 mmol), 4-dimethylaminopyridine (2.0 mg, 0.02 mmol), and acetic anhydride (50 μL, 0.32 mmol) were added and the resulting solution was stirred for 5 hours at room temperature. The reaction was then acidified with 10 mL 1N HCl, extracted with 10 mL ethyl acetate, washed with 10 mL 10% $NaHCO_3$, 10 mL brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash chromatography (3:1 ethyl acetate:hexanes) afforded a single β-pentaacetate isomer (7.8 mg, 0.020 mmol) in 35% overall yield. A comparison of the ^1H and ^{13}C NMR spectra of the above generated pentaacetate to an authentic sample of β-D-mannosamine pentaacetate generated by the method of O'Niel[15] showed the two samples to be identical.

2-Deoxy-2-acetylmercapto-4,6-bis-*O*-triisopropylsilyl-β-L-allopyranose. (16) In an inert atmosphere glove-box, a 2 dram flame-dried vial was charged with titanium (IV) chloride tetrahydrofuran complex (1:2) (231 mg, 0.69 mmol) and a magnetic stirbar. After removing the sealed vial from the glove-box and placing it under an argon atmosphere, 2.3 mL of dichloromethane was added and the solution was cooled to –20 °C. Then, a solution of (2*S,* 3*S*)-3-hydroxy-2,3-bis-triisopropylsilanoxy-propionaldehyde (100 mg, 0.23 mmol) in 2.3 mL of dichloromethane was added follwed by dropwise addition of (*Z*)-thioacetic acid *S*-[2-(trimethyl-silanyloxy)-vinyl] ester (231 mg, 1.16 mmol, 3:1 *Z*:*E*). After 16 hours at –20 °C, an additional 100 mg of the enolsilane was added and the solution was stirred for an additional 34 hours. The reaction was then acidified by the addition of 100 mL saturated aqueous NH_4Cl, extracted with

[15] O'Neill *Can.J.Chem.* **1959**, *37*, 1747.

ethyl acetate (3x50 mL), washed with 100 mL 10% $NaHCO_3$, 100 mL brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Crude ^1H NMR analysis indicated a >19:1 mixture of allose:mannose derived diastereomers as well as some minor acetal side-products. Flash chromatography (1:4 ether:hexanes + 1% triethylamine) afforded the title compound as a clear, colorless oil (90 mg, 0.16 mmol, stains blue in anisaldehyde, 3:1 α:β, 71%). IR (film) 3446, 2944, 2892, 2867, 1697, 1464, 1248, 1113, 1066, 883.5, 770.9, 682.1 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) α-anomer: δ 5.04 (br s, 1H, H1); 4.14 (m, 2H, H3 and H4); 3.99 (m, 2H, H6); 3.85 (m, 1H, H5); 3.79 (m, 1H, H2); 3.12 (s, 1H, C1 OH); 2.41 (s, 1H, C3 OH); 2.39 (s, 1H, $C(O)CH_3$); 1.15-1.06 (m, 42H, 6 $CH(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) α-anomer: δ 194.8, 93.3 (C1), 72.3 (C3), 68.23 (C5), 68.16 (C4), 62.7 (C6), 45.9 (C2), 30.8, 18.3, 18.3, 18.2, 18.2, 12.9, 12.4; β-anomer: δ 194.8, 94.7, 75.7, 72.3, 69.0, 63.3, 50.0, 30.8, 18.3, 18.3, 18.2, 18.2, 12.9, 12.4; 500 MHz COSY and HMQC spectra support the above ^1H and ^{13}C NMR assignments; HRMS (CI+) exact mass calcd for $[M\bullet]^+$ ($C_{26}H_{54}O_6Si_2S$) requires *m/z* 550.3180, found *m/z* 550.3153; $[\alpha]_D = -8.1$ (c = 2.00, $CHCl_3$, 3:1 α:β mixture).

2-*O*-Acetyl-4,6-bis-*O*-*tert*-butyldiphenylsilyl-α-L-allopyranose. (18) In an inert atmosphere glove-box, a 2 dram flame-dried vial was charged with titanium (IV) chloride tetrahydrofuran complex (1:2) (86.5 mg, 0.26 mmol) and a magnetic stirbar. After removing the sealed vial from the glove-box and placing it under an argon atmosphere, 0.865 mL of dichloromethane was added and the solution was cooled to –78 °C. Then, a solution of (2*S*, 3*S*)-3-hydroxy-2,3-bis-*tert*-butyl-diphenylsilanoxy-propionaldehyde (30.8 mg, 0.052 mmol) in 0.865 mL of dichloromethane was added follwed by dropwise addition of (*Z*)-acetic acid 2-(trimethyl-silanyloxy)-vinyl ester (75.3 mg, 0.43 mmol). After 2 hours at –78 °C, the reaction was warmed to –40 °C over 1 hour and then warmed to –20 °C for 10 hours. The reaction was then acidified by the addition of 100 mL saturated aqueous NH_4Cl, extracted with ethyl acetate (3x50 mL), washed with 100 mL 10% $NaHCO_3$, 100 mL brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo.* Crude ^1H NMR analysis indicated a >19:1 mixture of allose:mannose derived diastereomers as well as some minor acetal side-products. Flash chromatography (3:7 ethyl acetate:hexanes + 1% triethylamine) afforded the title compound as a clear, colorless oil (31.8 mg, 0.044 mmol, stains blue-green in anisaldehyde, 3:1 α:β, 86%). IR (film) 3406, 2944, 2867, 1742, 1464, 1374, 1236, 1050, 1014, 883.4, 681.6 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) α-

isomer: δ 7.64–7.31 (m, 20H, Ar-H); 5.12 (dd, 1H, *J* = 10.5, 3.5 Hz, H1); 5.06 (d, 1H, *J* = 10.5 Hz, C1 OH); 4.48 (ddd, 1H, *J* = 2.5, 2.5, 1.0 Hz, H2); 4.08 (m, 1H, H3); 4.13 (dd, 1H, *J* = 9.5, 3.0 Hz, H4); 3.79 (ddd, 1H, 9.5, 2.5, 2.5 Hz, H5); 3.91 (m, 2H, H6); 2.80 (s, 1H, C3 OH); 2.13 (s, 3H, $C(O)CH_3$); 1.02 (s, 18H, $C(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$) α-isomer: δ 170.3, 135.9, 134.1, 133.7, 132.8, 129.7, 128.4, 128.2, 127.7, 91.5, 71.5, 69.2, 69.1, 68.0, 63.7, 27.2, 21.2, 19.5; HRMS (FAB+) exact mass calcd for $[M+H]^+$ ($C_{40}H_{51}O_7Si_2$) requires *m/z* 699.3168, found *m/z* 699.3164; $[\alpha]_D = -20.3$ (c = 2.00, $CHCl_3$, 3:1 α:β mixture).

2-*O*-Acetyl-6-*O*-*tert*-butyldiphenylsilyl-4-deoxy-4-methyl-α-L-allopyranose. (19) In an inert atmosphere glove-box, a 2 dram flame-dried vial was charged with titanium (IV) chloride tetrahydrofuran complex (1:2) (140 mg, 0.42 mmol) and a magnetic stirbar. After removing the sealed vial from the glove-box and placing it under an argon atmosphere, 1.4 mL of dichloromethane was added and the solution was cooled to –78 °C. Then, a solution of (2*S,* 3*R*)-4-*tert*-butyldiphenyl-silanyloxy-3-hydroxy-2-methylbutanal (50 mg, 0.14 mmol) in 1.4 mL of dichloromethane was added follwed by dropwise addition of (*Z*)-acetic acid 2-(trimethyl-silanyloxy)-vinyl ester (75.3 mg, 0.43 mmol). After 1 hour at –78 °C, the reaction was warmed slowly to –30 °C over 3 hours and then kept at –30 °C for 3 additional hours. The reaction was then acidified by the addition of 100 mL saturated aqueous NH_4Cl, extracted with ethyl acetate (3x50 mL), washed with 100 mL 10% $NaHCO_3$, 100 mL brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Crude ^1H NMR analysis indicated a >19:1 mixture of allose:mannose derived diastereomers as well as some minor acetal side-products. Flash chromatography (2:3 ethyl acetate:hexanes + 1% triethylamine) afforded the title compound as a clear, colorless oil (36.5 mg, 0.080 mmol, stains blue-green in anisaldehyde, 4:1 α:β, 68%). IR (film) 3436, 2932, 2858, 1743, 1428, 1373, 1273, 1113, 1057, 848.3, 823.1, 739.5, 702.7, 613.6, 504.3 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) α-isomer: δ 7.72 (m, 4H, Ar-H); 7.43 (m, 6H, Ar-H); 5.25 (dd, 1H, *J* = 8.0, 2.5 Hz, H2); 4.78 (dd (apparent t), 1H, *J* = 3.5, 3.5 Hz, H1); 4.48 (m, 1H, H3); 4.11 (br s, 1H, C1-OH); 3.85 (m, 3H, H5, H6); 2.24 (m, 1H, H4); (m, 2H, H6); 2.19 (s, 3H, $C(O)CH_3$); 1.08 (s, 9H, $C(CH_3)_3$); 1.00 (d, 3H, *J* = 7.0 Hz, C4-CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) α-isomer: δ 170.4, 136.0, 135.9, 133.9, 133.6, 129.90, 129.87, 127.91, 127.85, 92.7, 72.5, 71.2, 69.1, 64.3, 35.3, 27.1, 21.3, 13.6; HRMS (FAB+) exact mass calcd for $[M+Na]^+$ ($C_{25}H_{34}O_6NaSi_2$) requires *m/z* 481.2022, found *m/z* 481.2007; $[\alpha]_D = -16.3$ (c = 2.00, $CHCl_3$, 4:1 α:β mixture).