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Dimethylthexylsilyl 2-acetamido-3-*O*-allyl-2-deoxy-6-*O*-(4-methoxybenzyl)- β -_D-glucopyranoside, dimethylthexylsilyl 3,4,6-tri-*O*-benzyl- β -_D-mannopyranosyl-(1 $\rightarrow$ 4)-2-acetamido-3-*O*-allyl-2-deoxy-6-*O*-(4-methoxybenzyl)- β -_D-glucopyranoside, and dimethylthexylsilyl 2-*O*-(benzylsulfonyl)-3,4,6-tri-*O*-benzyl- β -_D-mannopyranosyl-2-acetamido-3-*O*-allyl-2-deoxy-6-*O*-(4-methoxybenzyl)- β -_D-glucopyranoside: synthesis of authentic samples*

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Abstract

Dimethylthexylsilyl 2-acetamido-3-*O*-allyl-2-deoxy-6-*O*-(4-methoxybenzyl)- β -_D-glucopyranoside was prepared by reduction of the corresponding 4,6-*O*-(4-methoxybenzylidene) acetal with sodium cyanoborohydride and trifluoroacetic acid. This alcohol was coupled to 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl- α -_D-glucopyranosyl trichloroacetimidate to give a β -glucoside that was converted to dimethylthexylsilyl 3,4,6-tri-*O*-benzyl- β -_D-mannopyranosyl-(1 $\rightarrow$ 4)-2-acetamido-3-*O*-allyl-2-deoxy-6-*O*-(4-methoxybenzyl)- β -_D-glucopyranoside by saponification, Dess-Martin oxidation and sodium borohydride reduction. Sulfonylation then gave dimethylthexylsilyl 2-*O*-(benzylsulfonyl)-3,4,6-tri-*O*-benzyl- β -_D-mannopyranosyl-(1 $\rightarrow$ 4)-2-acetamido-3-*O*-allyl-2-deoxy-6-*O*-(4-methoxybenzyl)- β -_D-glucopyranoside.

Keywords

Glycosylation; Uloside; Mannoside

The NMR spectral data for dimethylthexylsilyl 2-acetamido-3-*O*-allyl-2-deoxy-6-*O*-(4-methoxybenzyl)- β -_D-glucopyranoside (**4**) and dimethylthexylsilyl 3,4,6-tri-*O*-benzyl- β -_D-mannopyranosyl-(1 $\rightarrow$ 4)-2-acetamido-3-*O*-allyl-2-deoxy-6-*O*-(4-methoxybenzyl)- β -_D-glucopyranoside (**11**), as described by Schmidt and co-workers,¹ is incorrect.^{2,3} We describe

*Supplementary data is available for this Note

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unambiguous syntheses of authentic samples of both compounds and of the 2-benzylsulfonyl derivative (**12**) of **11**, and provide full characterization data for all three compounds.

Synthesis of the glycosyl acceptor **4** began with the known dimethylthexylsilyl glycoside **1**⁴ from which the esters were removed with catalytic sodium methoxide to give a triol that was immediately converted to the 4-methoxybenzylidene acetal **2** (Scheme 1). The 3-*O*-allyl ether **6** was then obtained by treatment with sodium hydride and allyl bromide. Reductive cleavage of the 4-methoxybenzylidene acetal with sodium cyanoborohydride and trifluoroacetic acid⁵ finally gave the acceptor **4** in 70% yield together with 6% of the 4-*O*-(4-methoxybenzyl) ether **5** (Scheme 1). The regioselectivity of the reductive ring opening reaction is supported by the chemical shift (δ 70.7) of C-6 in the 6-*O*-(4-methoxybenzyl) isomer **4**, which is consistent of that of C-6 in a closely related compound, allyl 3-*O*-benzyl-2-deoxy-2-acetamido- β -D-glucopyranoside, which was accessed by a different route.⁶ Additional confirmation was obtained by acetylation of both **4** and **5**, giving **6** and **7**, respectively, when the anticipated chemical shift changes were observed in the NMR spectra.

Adapting the classical Lindberg approach to β -mannosides,^{7,8} 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl- α -D-glucopyranosyl trichloroacetimidate (**8**)⁹ was activated with trimethylsilyl triflate¹⁰ in the presence of **4**, leading to the isolation of the β -glucoside **9** in 51% yield (Scheme 2). Saponification gave the alcohol **10**, Dess-Martin oxidation¹¹ of which then provided a uloside that was immediately reduced with sodium borohydride to give the β -mannoside **11** in 84% yield along with 4.5% of the gluco-isomer **10**. Finally, sulfonylation of **11** with benzylsulfonyl chloride in pyridine gave **12** in 97% yield (Scheme 2).

1. Experimental

1.1. General Methods

Optical rotations were determined with an Autopol III polarimeter for solutions in CHCl_3 . NMR spectra were recorded for CDCl_3 solutions with a Varian 400 or 500 MHz spectrometer. Chemical shifts are in ppm downfield from tetramethylsilane. High resolution mass spectra were recorded with a Waters Micromass-LCT-Premier-XE instrument.

1.2. Dimethylthexylsilyl 2-Acetamido-4,6-di-*O*-(4-methoxybenzylidene)-2-deoxy- β -D-glucopyranoside (**2**)

To a solution of **1**⁴ (3.38 g, 6.89 mmol) in $\text{MeOH}-\text{CH}_2\text{Cl}_2$ (1:1 v:v, 30 mL) was added a solution of NaOMe in MeOH (25 wt%, 0.2 mL, 0.88 mmol). The resulting mixture was stirred for 2.5 h at ambient temp under N_2 atmosphere. Monitoring by TLC ($\text{MeOH}-\text{CH}_2\text{Cl}_2$ 1:4) indicated that the reaction went to completion. The reaction was neutralized with Amberlist-15 resin (H^+), filtered and the filtrate was concentrated to furnish a white foam, which was dissolved in DMF (20 mL). PPTS (184 mg, 0.73 mmol) and *p*-methoxybenzaldehyde dimethyl acetal (1.40 mL, 8.26 mmol) were added. The mixture was evaporated on a rotary evaporator at 50 °C to remove the methanol produced during the reaction. After 2 h TLC ($\text{EtOAc}-\text{hexane}$ 1:3) showed that the reactant was completely consumed. The mixture was poured into 1 N aq NaHCO_3 and extracted with CH_2Cl_2 . The organic phase was washed with brine, dried over Na_2SO_4 , and concentrated. The residue was subjected to silica gel column chromatography ($\text{EtOAc}-\text{CH}_2\text{Cl}_2$ 3:2 $\rightarrow$ 2:1) to give **2** (2.22 g, 4.62 mmol, 67%). $[\alpha]_D^{22} = -49.7$ (*c* 1.1); ^1H NMR (400 MHz) δ 7.40 (d, 2 H, $J = 8.8$ Hz, Ar-H), 6.86 (d, 2 H, $J = 8.0$ Hz, Ar-H), 5.83 (d, 1 H, $J = 6.7$ Hz, CH_3CONH), 5.47 (s, 1 H, PhCHO_2), 4.87 (d, 1 H, $J = 8.0$ Hz, H-1), 4.23 (dd, 1 H, $J = 3.2, 10.0$ Hz, H-6_a), 4.18 (br. s, 1 H, OH), 4.02 (t, 1 H, $J = 9.9$ Hz, H-3), 3.77 (s, 3 H, OCH_3), 3.73 (t, 1 H, $J = 10.2$ Hz, H-6_b), 3.52 (t, 1 H, $J = 9.2$ Hz, H-4), 3.48–3.40 (m, 2 H, H-5, H-2), 1.99 (s, 3 H, CH_3CONH), 1.65–1.58 (m, 1 H, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.88–0.84 (m, 12 H, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.15 (s, 3 H, SiCH_3), 0.14 (s, 3 H, SiCH_3); ^{13}C NMR (100 MHz)

δ 171.8, 160.4, 129.9, 127.9, 113.8, 102.0, 96.2, 81.9, 71.4, 68.8, 66.6, 61.0, 55.5, 34.2, 25.0, 23.8, 20.3, 20.2, 18.8, 18.7, -1.5, -3.2. ESIMS m/z Calcd for $C_{24}H_{39}NO_7SiNa$ [$M + Na^+$]: 504.2394. Found: 504.2407.

1.3. Dimethylthexylsilyl 2-Acetamido-3-O-allyl-4,6-di-O-(4-methoxybenzylidene)-2-deoxy- β -D-glucopyranoside (3)

To a solution of alcohol **2** (2.15 g, 4.46 mmol) in anhydr DMF (15 mL) was added 60% NaH in mineral oil (284 mg, 7.10 mmol) at 0 °C under N_2 atmosphere. After stirring for 10 min, allyl bromide (0.50 mL, 5.91 mmol) was added. The resulting mixture was stirred for 30 min at 0 °C, then was allowed to warm to ambient temperature and stirred for another 1.5 h. The mixture was poured into aq NH_4Cl and extracted with CH_2Cl_2 .

The organic phase was washed with brine, dried over Na_2SO_4 , and concentrated. The residue was subjected to silica gel column chromatography to furnish **3** (1.59 g, 3.04 mmol, 68%). $[\alpha]_D^{22} = -14.6$ (c 1.0); 1H NMR (400 MHz) δ 7.38 (d, 2 H, $J = 8.0$ Hz, Ar-H), 6.87 (d, 2 H, $J = 8.0$ Hz, Ar-H), 5.93 (br. s, 1 H, CH_3CONH), 5.89–5.81 (m, 1 H, $CH_2CH=CH_2$), 5.46 (s, 1 H, $ArCHO_2$), 5.23–5.16 (m, 2 H, H-1, $CH_2CH=CH_2$), 5.10 (d, 1 H, $J = 10.4$ Hz, $CH_2CH=CH_2$), 4.31 (dd, 1 H, $J = 5.6$, 13.2 Hz, $CH_2CH=CH_2$), 4.24 (dd, 1 H, $J = 4.8$, 10.8 Hz, H-6_a), 4.14–4.07 (m, 2 H, $CH_2CH=CH_2$, H-3), 3.78 (s, 3 H, OCH_3), 3.72 (t, 1 H, $J = 10.6$ Hz, H-6_b), 3.58 (t, 1 H, $J = 9.0$ Hz, H-4), 3.50–3.44 (m, 1 H, H-5), 3.24–3.21 (m, 1 H, H-2), 1.95 (s, 3 H, CH_3CONH), 1.62–1.57 (m, 1 H, $SiC(CH_3)_2CH(CH_3)_2$), 0.86 (s, 3 H, $SiC(CH_3)_2CH(CH_3)_2$), 0.85 (s, 3 H, $SiC(CH_3)_2CH(CH_3)_2$), 0.83 (s, 6 H, $SiC(CH_3)_2CH(CH_3)_2$), 0.13 (s, 3 H, $SiCH_3$), 0.12 (s, 3 H, $SiCH_3$); ^{13}C NMR (100 MHz) δ 170.4, 160.2, 135.3, 130.2, 127.6, 117.1, 113.8, 101.3, 95.5, 82.7, 76.8, 73.5, 69.0, 66.2, 60.2, 55.5, 34.2, 25.0, 23.8, 20.2, 18.8, -1.6, -3.2. ESIMS m/z Calcd for $C_{27}H_{43}NO_7SiNa$ [$M + Na^+$]: 544.2693. Found: 544.2693.

1.4. Dimethylthexylsilyl 2-Acetamido-3-O-allyl-2-deoxy-6-O-(4-methoxybenzyl)- β -D-glucopyranoside (4) and Dimethylthexylsilyl 2-Acetamido-3-O-allyl-2-deoxy-4-O-(4-methoxybenzyl)- β -D-glucopyranoside (5)

To a solution of **3** (1.59 g, 3.04 mmol), in anhydr DMF (22 mL) in the presence of 4 Å MS was added $NaBH_3CN$ (1.91 g, 30.4 mmol) followed by a solution of TFA (4.70 mL, 61 mmol) in anhydr DMF (24 mL) at 0 °C over 25 min. After 1 h at 0 °C, the reaction mixture was warmed to room temperature and stirred for another 4 h. At this point the reaction mixture was poured into H_2O (500 mL) and solid $NaHCO_3$ was slowly added to neutralize the mixture to pH = 7.0. The water phase was extracted with CH_2Cl_2 (3 $\times$ 100 mL). The collected organic phase was washed with brine, dried over Na_2SO_4 and concentrated. The resulting residue was purified by flash chromatography on silica gel to afford **4** (1.11 g, 2.12 mmol, 70%) and **5** (90.5 mg, 0.17 mmol, 6%).

For **4** $[\alpha]_D^{21} = -20.5$ (c 0.8); 1H NMR (400 MHz) δ 7.23 (d, 2 H, $J = 8.0$ Hz, Ar-H), 6.85 (d, 1 H, $J = 8.8$ Hz, Ar-H), 5.92–5.83 (m, 1 H, $CH_2CH=CH_2$), 5.72 (d, 1 H, $J = 7.2$ Hz, CH_3CONH), 5.24 (d, 1 H, $J = 17.2$ Hz, $CH_2CH=CH_2$), 5.13 (d, 1 H, $J = 9.6$ Hz, $CH_2CH=CH_2$), 5.02 (d, 1 H, $J = 7.2$ Hz, H-1), 4.53–4.46 (m, 2 H, $ArCH_2O$), 4.24 (dd, 1 H, $J = 5.6$, 13.2 Hz, $CH_2CH=CH_2$), 4.15 (dd, 1 H, $J = 6.0$, 13.2 Hz, $CH_2CH=CH_2$), 3.85 (t, 1 H, $J = 10.0$ Hz, H-3), 3.79 (s, 3 H, OCH_3), 3.69 (d, 2 H, $J = 4.8$ Hz, H-6_a, H-6_b), 3.56 (t, 1 H, $J = 8.8$ Hz, H-4), 3.51–3.46 (m, 1 H, H-5), 3.25–3.20 (m, 1 H, H-2), 3.08 (br. s, 1 H, OH), 1.94 (s, 3 H, CH_3CONH), 1.63–1.56 (m, 1 H, $SiC(CH_3)_2CH(CH_3)_2$), 0.86 (s, 3 H, $SiC(CH_3)_2CH(CH_3)_2$), 0.84 (s, 3 H, $SiC(CH_3)_2CH(CH_3)_2$), 0.82 (s, 6 H, $SiC(CH_3)_2CH(CH_3)_2$), 0.14 (s, 3 H, $SiCH_3$), 0.11 (s, 3 H, $SiCH_3$); ^{13}C NMR (100 MHz) δ 170.4, 159.5, 135.4, 130.2, 129.5, 117.2, 114.0, 95.2, 80.6, 77.6, 74.0, 73.5, 73.2, 59.2, 55.5, 34.1, 25.0, 23.8, 20.1, 18.7, -1.6, -3.3. ESIMS m/z Calcd for $C_{27}H_{45}NO_7SiNa$ [$M + Na^+$]: 546.2851. Found: 546.2863.

For **5** $[\alpha]_D^{21} = +5.2$ (c 0.6); ^1H NMR (500 MHz) δ 7.23 (d, 2 H, $J = 8.5$ Hz, Ar-H), 6.85 (d, 1 H, $J = 8.0$ Hz, Ar-H), 5.92–5.86 (m, 1 H, $\text{CH}_2\text{CH}=\text{CH}_2$), 5.84 (d, 1 H, $J = 8.5$ Hz, CH_3CONH), 5.24 (d, 1 H, $J = 17.0$ Hz, $\text{CH}_2\text{CH}=\text{CH}_2$), 5.14 (d, 1 H, $J = 10.5$ Hz, $\text{CH}_2\text{CH}=\text{CH}_2$), 5.02 (d, 1 H, $J = 7.5$ Hz, H-1), 4.73 (d, 1 H, $J = 10.5$ Hz, ArCH_2O), 4.54 (d, 1 H, $J = 11.0$ Hz, ArCH_2O), 4.28 (dd, 1 H, $J = 5.0, 12.5$ Hz, $\text{CH}_2\text{CH}=\text{CH}_2$), 4.14 (dd, 1 H, $J = 6.0, 13.0$ Hz, $\text{CH}_2\text{CH}=\text{CH}_2$), 3.93 (t, 1 H, $J = 10.0$ Hz, H-3), 3.78 (s, 4 H, OCH_3 , H-6_a), 3.64–3.62 (m, 1 H, H-6_b), 3.45 (t, 1 H, $J = 9.5$ Hz, H-4), 3.42–3.38 (m, 1 H, H-5), 3.30–3.25 (m, 1 H, H-2), 1.98 (s, 3 H, CH_3CONH), 1.63–1.56 (m, 1 H, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.86 (s, 3 H, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.84 (s, 3 H, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.82 (s, 6 H, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.14 (s, 3 H, SiCH_3), 0.10 (s, 3 H, SiCH_3); ^{13}C NMR (125 MHz) δ 170.4, 159.6, 135.3, 130.4, 129.9, 117.0, 114.1, 95.2, 80.8, 78.3, 75.2, 74.6, 73.7, 62.5, 59.6, 55.5, 34.2, 25.0, 23.8, 20.2, 18.7, –1.5, –3.2. ESIMS m/z Calcd for $\text{C}_{27}\text{H}_{45}\text{NO}_7\text{SiNa}$ [$\text{M} + \text{Na}^+$]: 546.2863. Found: 546.2863

1.5. Dimethylthexylsilyl 2-Acetamido-4-O-acetyl-3-O-allyl-2-deoxy-6-O-(4-methoxybenzyl)- β -D-glucopyranoside (**6**)

To a solution of **4** (65.0 mg, 124 μmol) in anhydrous pyridine (1 mL) was added Ac_2O (80.0 μL , 846 μmol). The resulting mixture was stirred for 4 h at room temperature under N_2 atmosphere. The reaction was quenched with MeOH and the volatiles were removed under reduced pressure. The residue was dissolved in CH_2Cl_2 and washed with 0.1 N HCl, satd. NaHCO_3 and brine. The organic phase was dried over Na_2SO_4 and concentrated. The residue was subjected to silica gel column chromatography (EtOAc–hexane 2:3) to afford acetate **6** (63.9 mg, 113 μmol , 91%) as a syrup. $[\alpha]_D^{22} = +15.1$ (c 1.1); ^1H NMR (500 MHz) δ 7.22 (d, 2 H, $J = 8.5$ Hz, Ar-H), 6.84 (d, 2 H, $J = 9.0$ Hz, Ar-H), 5.82–5.74 (m, 2 H, CH_3CONH , $\text{CH}_2\text{CH}=\text{CH}_2$), 5.21–5.15 (m, 2 H, H-1, $\text{CH}_2\text{CH}=\text{CH}_2$), 5.10 (dd, 1 H, $J = 1.5, 10.5$ Hz, $\text{CH}_2\text{CH}=\text{CH}_2$), 4.89 (t, 1 H, $J = 9.5$ Hz, H-4), 4.43 (s, 2 H, Ar-CH_2), 4.17 (t, 1 H, $J = 9.5$ Hz, H-3), 4.06–4.04 (m, 2 H, $\text{CH}_2\text{CH}=\text{CH}_2$), 3.78 (s, 3 H, OCH_3), 3.63–3.59 (m, 1 H, H-5), 3.49–3.48 (m, 2 H, H-6_a, H-6_b), 3.14–3.09 (m, 1 H, H-2), 1.96 (s, 3 H, CH_3COO), 1.94 (s, 3 H, CH_3CONH), 1.64–1.58 (m, 1 H, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.86 (d, 3 H, $J = 2.0$ Hz, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.85 (d, 3 H, $J = 2.0$ Hz, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.83 (s, 3 H, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.82 (s, 3 H, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.16 (s, 3 H, SiCH_3), 0.12 (s, 3 H, SiCH_3); ^{13}C NMR (125 MHz) δ 170.5, 170.0, 159.4, 134.9, 130.4, 129.5, 116.9, 113.9, 94.6, 77.8, 73.3, 72.8, 72.1, 69.9, 60.2, 55.5, 34.3, 25.0, 23.8, 21.2, 20.3, 18.8, –1.6, –3.3. ESIMS m/z Calcd for $\text{C}_{29}\text{H}_{47}\text{NO}_8\text{SiNa}$ [$\text{M} + \text{Na}^+$]: 588.2969. Found: 588.2970

1.6. Dimethylthexylsilyl 2-Acetamido-6-O-acetyl-3-O-allyl-2-deoxy-4-O-(4-methoxybenzyl)- β -D-glucopyranoside (**7**)

Following a similar protocol for **6**, **5** (87.2 mg, 166 μmol) was allowed to react with Ac_2O (100 μL , 1.1 mmol) in pyridine (1 mL) to furnish **7** (78.0 mg, 138 μmol , 83%) as a syrup. $[\alpha]_D^{22} = +20.8$ (c 1.1); ^1H NMR (500 MHz) δ 7.22 (d, 2 H, $J = 8.5$ Hz, Ar-H), 6.85 (d, 2 H, $J = 8.5$ Hz, Ar-H), 5.94–5.86 (m, 1 H, $\text{CH}_2\text{CH}=\text{CH}_2$), 5.80–5.76 (m, 1 H, CH_3CONH), 5.25 (dd, 1 H, $J = 1.5, 17.5$ Hz, $\text{CH}_2\text{CH}=\text{CH}_2$), 5.14 (d, 1 H, $J = 10.5$ Hz, $\text{CH}_2\text{CH}=\text{CH}_2$), 4.97 (d, 1 H, $J = 8.0$ Hz, H-1), 4.73 (d, 1 H, $J = 10.5$ Hz, Ar-CH_2), 4.48 (d, 1 H, $J = 10.5$ Hz, ArCH_2), 4.30–4.25 (m, 2 H, $\text{CH}_2\text{CH}=\text{CH}_2$, H-6_a), 4.17–4.10 (m, 2 H, $\text{CH}_2\text{CH}=\text{CH}_2$, H-6_b), 3.95 (t, 1 H, $J = 9.5$ Hz, H-3), 3.78 (s, 3 H, OCH_3), 3.54–3.51 (m, 1 H, H-5), 3.38 (t, 1 H, $J = 9.0$ Hz, H-4), 3.31–3.26 (m, 1 H, H-2), 2.01 (s, 3 H, CH_3COO), 1.94 (s, 3 H, CH_3CONH), 1.61–1.56 (m, 1 H, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.85 (d, 3 H, $J = 1.5$ Hz, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.83 (d, 3 H, 1.0 Hz, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.81 (s, 3 H, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.80 (s, 3 H, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.11 (s, 3 H, SiCH_3), 0.10 (s, 3 H, SiCH_3); ^{13}C NMR (125 MHz) δ 171.0, 170.3, 159.6, 135.2, 130.1, 130.0, 117.1, 114.1, 95.0, 80.8, 78.2, 74.4, 73.7, 73.0, 63.6, 59.5, 55.5, 34.3, 25.0, 23.8, 21.0, 20.3, 20.2, 18.7, –1.7, –3.3. ESIMS m/z Calcd for $\text{C}_{29}\text{H}_{47}\text{NO}_8\text{SiNa}$ [$\text{M} + \text{Na}^+$]: 588.2969. Found: 588.2967

1.7. Dimethylthexylsilyl 2-O-Benzoyl-3,4,6-tri-O-benzyl- β -D-glucopyranosyl-(1 $\rightarrow$ 4)-2-acetamido-3-O-allyl-2-deoxy-6-O-(4-methoxybenzyl)- β -D-glucopyranoside (9)

A solution of **4** (253 mg, 483 μ mol) in CH_2Cl_2 (15 mL) was stirred for 2 h in the presence of 5Å MS (820 mg) at ambient temperature under N_2 atmosphere after which TMSOTf (48 μ L, 265 μ mol) was added followed by a solution of **8**⁹ (605.8 mg, 867 mmol) in CH_2Cl_2 (8 mL) over 1.5 h. The mixture was stirred for another 2.5 h until TLC (EtOAc–hexane 2:3) showed that the reactant was completely consumed. The reaction mixture was diluted with CH_2Cl_2 and the solid was filtered off. The filtrate was washed with satd. aq NaHCO_3 and brine. The collected organic phase was dried over Na_2SO_4 and concentrated. The resulting residue was purified by flash chromatography (EtOAc–hexane 2:5) on silica gel to afford disaccharide **9** (260.0 mg, 245 μ mol, 51%). $[\alpha]_{\text{D}}^{21} = +13.1$ (c 0.8); ^1H NMR (500 MHz) δ 7.97 (d, 2 H, $J = 7.5$ Hz, Ar-H), 7.58 (t, 1 H, $J = 7.5$ Hz, Ar-H), 7.46–7.57 (t, 2 H, $J = 8.0$ Hz, Ar-H), 7.38–7.11 (m, 17 H, Ar-H), 6.88 (d, 2 H, $J = 8.5$ Hz, Ar-H), 5.88–5.82 (m, 2 H, CH_3CONH), $\text{CH}_2\text{CH}=\text{CH}_2$, 5.24–5.18 (m, 2 H, $\text{H}''\text{-2}$, $\text{CH}_2\text{CH}=\text{CH}_2$), 5.05 (d, 1 H, $J = 10.5$ Hz, $\text{CH}_2\text{CH}=\text{CH}_2$), 4.81 (d, 1 H, $J = 10.5$ Hz, ArCH_2), 4.76 (d, 1 H, $J = 6.5$ Hz, $\text{H}'\text{-1}$), 4.74 (d, 1 H, $J = 11.5$ Hz, ArCH_2), 4.66–4.52 (m, 6 H, $\text{H}''\text{-1}$, ArCH_2), 4.31 (d, 1 H, $J = 11.5$ Hz, ArCH_2), 4.28 (dd, 1 H, $J = 5.0$, 13.0 Hz, $\text{CH}_2\text{CH}=\text{CH}_2$), 4.11 (dd, 1 H, $J = 5.5$, 13.0 Hz, $\text{CH}_2\text{CH}=\text{CH}_2$) 3.96 (t, 1 H, $J = 7.0$ Hz, $\text{H}'\text{-3}$), 3.83–3.69 (m, 8 H, OCH_3 , $\text{H}'\text{-4}$, $\text{H}'\text{-6}_a$, $\text{H}'\text{-6}_b$, $\text{H}''\text{-6}_a$, $\text{H}''\text{-6}_b$), 3.58–3.53 (m, 3 H, $\text{H}''\text{-3}$, $\text{H}''\text{-4}$, $\text{H}'\text{-5}$), 3.46–3.42 (m, 1 H, $\text{H}''\text{-5}$), 3.41–3.38 (m, 1 H, $\text{H}'\text{-2}$), 1.99 (s, 3 H, CH_3CONH), 1.59–1.54 (m, 1 H, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.84 (d, 3 H, $J = 2.5$ Hz, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.82 (d, 3 H, $J = 2.5$ Hz, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.78 (s, 3 H, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.77 (s, 3 H, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.03 (s, 3 H, SiCH_3), -0.02 (s, 3 H, SiCH_3); ^{13}C NMR (125 MHz, CDCl_3) δ 170.1, 165.6, 159.5, 138.4, 138.3, 138.1, 135.6, 133.5, 130.6, 130.0, 129.8, 128.7, 128.6, 128.5, 128.2, 128.1, 128.0, 127.8, 116.5, 114.1, 99.9 ($\text{C}_{1'}$, $J_{\text{C}_{1'}\text{-H}_{1'}} = 163.4$), 95.2 ($\text{C}_{1'}$, $J_{\text{C}_{1'}\text{-H}_{1'}} = 164.2$), 83.1, 78.3, 78.2, 75.4, 75.2, 74.6, 74.4, 73.8, 73.3, 72.6, 68.9, 68.8, 56.5, 55.4, 34.2, 25.0, 23.7, 20.3, 18.8, -1.8 , -3.4 . ESIMS m/z Calcd for $\text{C}_{61}\text{H}_{77}\text{NO}_{13}\text{SiNa}$ [$\text{M} + \text{Na}^+$]: 1082.5062. Found: 1082.5066.

1.8. Dimethylthexylsilyl 3,4,6-Tri-O-benzyl- β -D-glucopyranosyl-(1 $\rightarrow$ 2)-acetamido-3-O-allyl-2-deoxy-6-O-(4-methoxybenzyl)- β -D-glucopyranoside (10)

To a solution of **9** (160.0 mg, 151 μ mol) in MeOH–THF (1:1, v:v, 6 mL) was added a solution of NaOMe in MeOH (25 wt%, 150 μ L, 656 μ mol). The resultant mixture was stirred for 18 h at ambient temperature under N_2 atmosphere. Monitoring by TLC (MeOH– CH_2Cl_2 1:4) indicated that the reaction went to completion. The reaction was neutralized with Amberlite IR-120 resin (H^+), filtered and the filtrate was concentrated. The residue was purified by flash chromatography on silica gel (EtOAc– CH_2Cl_2 1:5) to furnish alcohol **10** (110.5 mg, 116 μ mol, 77%). $[\alpha]_{\text{D}}^{21} = +17.5$ (c 1.3); ^1H NMR (500 MHz) δ 7.39–7.27 (m, 15 H, Ar-H), 7.17 (d, 2 H, $J = 7.5$ Hz, Ar-H), 6.87 (d, 2 H, $J = 9.0$ Hz, Ar-H), 5.88–5.81 (m, 1 H, $\text{CH}_2\text{CH}=\text{CH}_2$), 5.75 (d, 1 H, $J = 7.5$ Hz, CH_3CONH), 5.19 (d, 1 H, $J = 12.5$ Hz, $\text{CH}_2\text{CH}=\text{CH}_2$), 5.06–5.03 (m, 2 H, $\text{CH}_2\text{CH}=\text{CH}_2$, $\text{H}'\text{-1}$), 4.94 (d, 1 H, $J = 11.5$ Hz, ArCH_2), 4.84–4.80 (m, 2 H, ArCH_2), 4.62 (d, 1 H, $J = 12.0$ Hz, ArCH_2), 4.58–4.47 (m, 5 H, ArCH_2 , $\text{H}''\text{-1}$), 4.45 (dd, 1 H, $J = 5.0$, 12.5 Hz, $\text{CH}_2\text{CH}=\text{CH}_2$), 4.08–4.02 (m, 2 H, $\text{CH}_2\text{CH}=\text{CH}_2$, $\text{H}'\text{-3}$), 3.96–3.91 (m, 2 H, $\text{H}'\text{-4}$, $\text{H}'\text{-6}_a$), 3.76 (s, 3 H, OCH_3), 3.70–3.66 (m, 3 H, $\text{H}'\text{-6}_b$, $\text{H}''\text{-6}_a$, $\text{H}''\text{-6}_b$), 3.63–3.59 (m, 2 H, $\text{H}''\text{-4}$, OH), 3.52–3.45 (m, 3 H, $\text{H}''\text{-2}$, $\text{H}''\text{-3}$, $\text{H}'\text{-5}$), 3.42–3.39 (m, 1 H, $\text{H}''\text{-5}$), 3.25–3.20 (m, 1 H, $\text{H}'\text{-2}$), 1.94 (s, 3 H, CH_3CONH), 1.65–1.60 (m, 1 H, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.88 (d, 3 H, $J = 2.5$ Hz, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.87 (d, 3 H, $J = 2.5$ Hz, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.84 (s, 3 H, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.83 (s, 3 H, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.16 (s, 3 H, SiCH_3), 0.12 (s, 3 H, SiCH_3); ^{13}C NMR (125 MHz) δ 170.3, 159.5, 139.1, 138.5, 138.4, 135.7, 129.9, 128.6, 128.5, 128.2, 128.1, 128.0, 127.9, 127.8, 116.2, 114.0, 103.4 ($\text{C}_{1'}$, $J_{\text{C}_{1'}\text{-H}_{1'}} = 165.7$), 95.0 ($\text{C}_{1'}$, $J_{\text{C}_{1'}\text{-H}_{1'}} = 164.1$), 84.8, 79.5, 77.7, 76.1, 75.3, 75.2, 74.4, 73.7, 73.6, 73.3, 69.1, 68.9, 59.1, 55.4, 34.3, 25.0, 23.8, 20.3, 18.8, -1.6 , -3.2 . ESIMS m/z Calcd for $\text{C}_{54}\text{H}_{73}\text{NO}_{12}\text{SiNa}$ [$\text{M} + \text{Na}^+$]: 978.4800. Found: 978.4823

1.9. Dimethylthexylsilyl 3,4,6-Tri-O-benzyl- β -D-mannopyranosyl-(1 $\rightarrow$)-2-acetamido-3-O-allyl-2-deoxy-6-O-(4-methoxybenzyl)- β -D-glucopyranoside (**11**)

To a solution of **10** (110.5 mg, 116 μ mol) in CH_2Cl_2 (6 mL) was added Dess-Martin periodinane (97 mg, 229 μ mol). The resulting mixture was stirred for 2 h at ambient temperature under N_2 temperature. Monitoring by TLC (EtOAc–hexane 1:1) showed the reaction went to completion. The mixture was diluted with CH_2Cl_2 , washed with aq NaHCO_3 containing $\text{Na}_2\text{S}_2\text{O}_3$ and brine. The organic phase was dried over Na_2SO_4 and concentrated. The resulting residue was dissolved in $\text{MeOH}-\text{CH}_2\text{Cl}_2$ (1:1, v:v, 6 mL). The solution was cooled to 0 $^\circ\text{C}$, and NaBH_4 (58 mg, 1.5 mmol) was added. The resulting mixture was stirred for 12 h while the temperature was elevated to the ambient. TLC (EtOAc– CH_2Cl_2 1:1) showed that the reaction went to completion. The reaction was quenched with AcOH and concentrated. The residue was diluted with CH_2Cl_2 and washed with brine. The organic phase was dried over Na_2SO_4 and concentrated. The residue was applied to silica gel column (EtOAc– CH_2Cl_2 1:2) to afford **11** (92.3 mg, 97 μ mol, 84%) and **10** (5.0 mg, 5.2 μ mol, 4.5%).

11: $[\alpha]_D^{21} = +2.8$ (*c* 1.0); ^1H NMR (500 MHz) δ 7.36–7.20 (m, 17 H, Ar-H), 6.85 (d, 2 H, *J* = 8.5 Hz, Ar-H), 5.94 (d, 1 H, *J* = 8.0 Hz, CH_3CONH), 5.87–5.81 (m, 1 H, $\text{CH}_2=\text{CHCH}_2$), 5.19 (d, 1 H, *J* = 12.5 Hz, $\text{CH}_2=\text{CHCH}_2$), 5.05 (d, 1 H, *J* = 10.0 Hz, $\text{CH}_2=\text{CHCH}_2$), 5.02 (d, 1 H, *J* = 6.5 Hz, H'-1), 4.86 (d, 1 H, *J* = 11.0 Hz, ArCH_2), 4.67 (d, 1 H, *J* = 12.0 Hz, ArCH_2), 4.61 (s, 1 H, H''-1), 4.58–4.51 (m, 5 H, ArCH_2), 4.43 (d, 1 H, *J* = 11.5 Hz, ArCH_2), 4.28 (dd, 1 H, *J* = 5.5, 12.5 Hz, $\text{CH}_2=\text{CHCH}_2$), 4.10 (dd, 1 H, *J* = 6.0, 12.5 Hz, $\text{CH}_2=\text{CHCH}_2$), 4.03 (d, 1 H, *J* = 3.0 Hz, H''-2), 3.99 (t, 1 H, *J* = 8.0 Hz, H'-3), 3.93 (t, 1 H, *J* = 8.0 Hz, H'-4), 3.87 (t, 1 H, *J* = 9.5 Hz, H''-4), 3.77–3.69 (m, 7 H, OCH_3 , H'-6_a, H'-6_b, H''-6_a, H''-6_b), 3.60–3.57 (m, 1 H, H'-5), 3.47–3.42 (m, 2 H, H'-2, H''-3), 3.36–3.33 (m, 1 H, H''-5), 2.60 (br. s, 1 H, OH), 1.94 (s, 3 H, CH_3CONH), 1.66–1.60 (m, 1 H, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.87 (d, 3 H, *J* = 2.5 Hz, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.86 (d, 3 H, *J* = 2.5 Hz, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.84 (s, 6 H, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.15 (s, 3 H, SiCH_3), 0.13 (s, 3 H, SiCH_3); ^{13}C NMR (125 MHz) δ 170.2, 159.4, 138.5, 138.4, 135.6, 130.4, 129.6, 128.7, 128.6, 128.5, 128.3, 128.1, 127.9, 127.7, 116.6, 114.1, 100.0 ($\text{C}_{1'}$, $J_{\text{C}_{1'}-\text{H}_{1'}} = 160.6$), 95.0 ($\text{C}_{1'}$, $J_{\text{C}_{1'}-\text{H}_{1'}} = 165.0$), 81.9, 78.6, 76.0, 75.6, 75.4, 74.7, 74.3, 73.7, 73.4, 73.0, 71.6, 69.4, 68.1, 57.8, 55.4, 34.3, 25.0, 23.8, 20.3, 18.8, -1.7, -3.2. ESIMS *m/z* Calcd for $\text{C}_{54}\text{H}_{73}\text{NO}_{12}\text{SiNa}$ [*M* + Na^+]: 978.4800. Found: 978.4818

1.10. Dimethylthexylsilyl 2-O-(Benzylsulfonyl)-3,4,6-tri-O-benzyl- β -D-mannopyranosyl-(1 $\rightarrow$)-2-acetamido-3-O-allyl-2-deoxy-6-O-(4-methoxybenzyl)- β -D-glucopyranoside (**12**)

To a solution of **11** (89.0 mg, 93 μ mol) in pyridine (2 mL) was added benzylsulfonyl chloride (31.0 mg, 162 μ mol) at 0 $^\circ\text{C}$ under N_2 atmosphere. After stirring 7 h, TLC (EtOAc–hexane 1:1) showed that the reaction went to completion. The reaction was diluted with CH_2Cl_2 , washed with 0.1 N HCl, satd. NaHCO_3 and brine. The combined organic phase was dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (EtOAc–hexane 2:3) to afford sulfonate **12** (100 mg, 90 μ mol, 97%) as a syrup. $[\alpha]_D^{22} = -43.6$ (*c* 0.8); ^1H NMR (500 MHz) δ 7.42–7.26 (m, 22 H, Ar-H), 6.85 (d, 2 H, *J* = 9.0 Hz, Ar-H), 5.93 (d, 1 H, *J* = 8.5 Hz, CH_3CONH), 5.84–5.78 (m, 1 H, $\text{CH}_2=\text{CHCH}_2$), 5.17 (d, 1 H, *J* = 17.0 Hz, $\text{CH}_2=\text{CHCH}_2$), 5.11 (d, 1 H, *J* = 2.0 Hz, H''-2), 5.03 (d, 1 H, *J* = 10.5 Hz, $\text{CH}_2=\text{CHCH}_2$), 4.93 (d, 1 H, *J* = 7.5 Hz, H'-1), 4.90 (d, 1 H, *J* = 10.5 Hz, ArCH_2), 4.76 (d, 1 H, *J* = 11.0 Hz, ArCH_2), 4.63–4.49 (m, 6 H, ArCH_2 , H''-1), 4.43 (d, 1 H, *J* = 12.0 Hz, ArCH_2), 4.38 (s, 2 H, ArCH_2SO_2), 4.22 (dd, 1 H, *J* = 5.0, 13.0 Hz, $\text{CH}_2=\text{CHCH}_2$), 4.13 (dd, 1 H, *J* = 5.5, 13.0 Hz, $\text{CH}_2=\text{CHCH}_2$), 3.97 (t, 1 H, *J* = 6.0 Hz, H'-3), 3.81–3.65 (m, 11 H, OCH_3 , H'-2, H'-4, H'-5, H'-6_a, H'-6_b, H''-4, H''-6_a, H''-6_b), 3.53–3.50 (dd, 1 H, *J* = 3.0, 9.5 Hz, H''-3), 3.34–3.32 (m, 1 H, H''-5), 1.80 (s, 3 H, CH_3CONH), 1.64–1.60 (m, 1 H, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.88–0.84 (m, 12 H, $\text{SiC}(\text{CH}_3)_2\text{CH}(\text{CH}_3)_2$), 0.15 (s, 3 H, SiCH_3), 0.14 (s, 3 H, SiCH_3); ^{13}C NMR (125 MHz) δ 170.1, 159.5, 138.5, 138.3, 137.4, 135.7, 131.1, 130.5, 129.7, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.8, 116.4, 114.1, 98.3 ($\text{C}_{1'}$),

$J_{\text{C1}''\text{-H1}''} = 160.4$), 95.3 ($\text{C1}'$, $J_{\text{C1}'\text{-H1}'} = 163.4$), 80.3, 79.0, 77.8, 75.9, 75.6, 75.5, 74.3, 73.8, 73.4, 72.8, 72.1, 69.8, 69.1, 57.9, 56.6, 55.4, 34.3, 25.0, 23.4, 20.3, 18.8, -1.7, -3.2. ESIMS m/z Calcd for $\text{C}_{61}\text{H}_{79}\text{NO}_{14}\text{SiNa}$ $[\text{M} + \text{Na}^+]$: 1132.4888. Found: 1132.4905.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

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Scheme 1.
Synthesis of acceptor **4**

Scheme 2.
Unambiguous synthesis of the β -mannosides **11** and **12**