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Note

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→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-(1→4)-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→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→4)-2-acetamido-3-*O*-allyl-2-deoxy-6-*O*-(4-methoxybenzyl)-β-D-glucopyranoside.

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→4)-2-acetamido-3-*O*-allyl-2-deoxy-6-*O*-(4-methoxybenzyl)-β-D-glucopyranoside (**11**), as described by Schmidt and co-workers,[1] are incorrect.[2,3] We describe 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 acid[5] 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 to 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 triflate[10] 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 oxidation[11] 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).

☆ Supplementary data is available for this Note.

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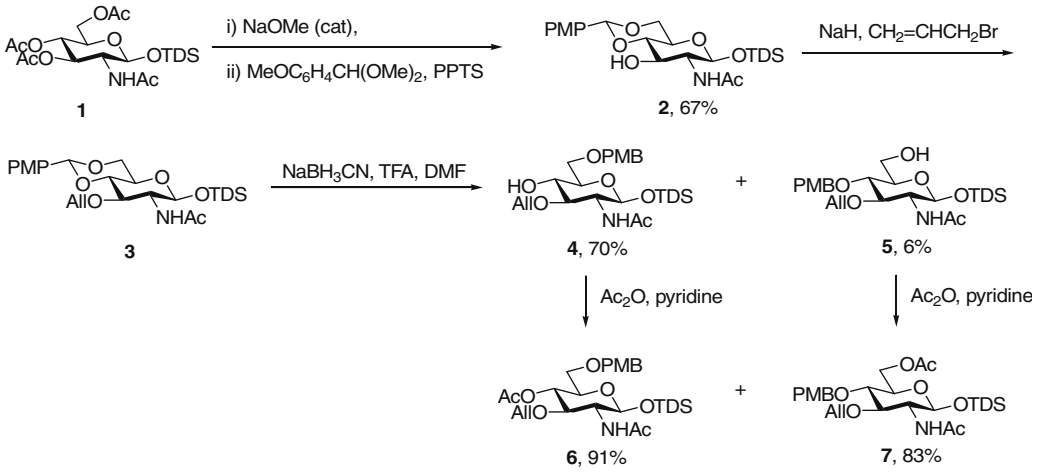
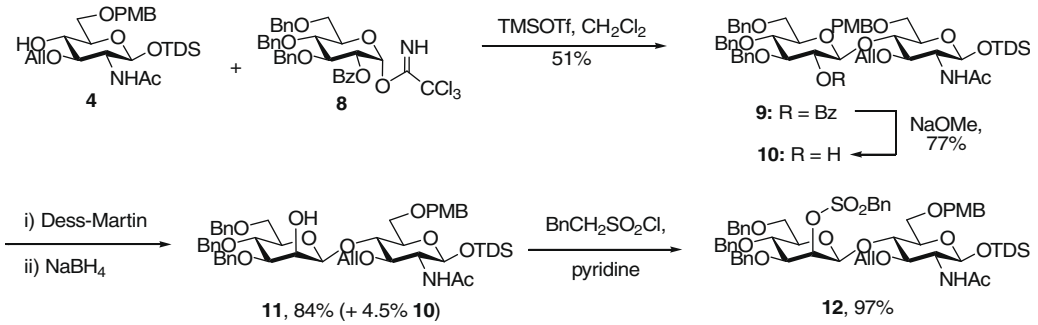


Scheme 1. Synthesis of acceptor **4**.



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

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 MeOH–CH_2Cl_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 (MeOH–CH_2Cl_2 1:4) indicated that the reaction went to completion. The reaction mixture 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 (EtOAc–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 (EtOAc–CH_2Cl_2 3:2→2:1) to give **2** (2.22 g, 4.62 mmol, 67%). $[\alpha]_D^{22}$ −49.7 (*c* 1.1); ^{1}H NMR (400 MHz) δ 7.40 (d, 2H, J = 8.8 Hz, Ar-H), 6.86 (d, 2H, J = 8.0 Hz, Ar-H), 5.83 (d, 1H, J = 6.7 Hz, CH_3CONH), 5.47 (s, 1H, $PhCHO_2$), 4.87 (d, 1H, J = 8.0 Hz, H-1), 4.23 (dd, 1H, J = 3.2, 10.0 Hz, H-6_a), 4.18 (br s, 1H, OH), 4.02 (t, 1H, J = 9.9 Hz, H-3), 3.77 (s, 3H, OCH_3), 3.73 (t, 1H, J = 10.2 Hz, H-6_b), 3.52 (t, 1H, J = 9.2 Hz, H-4), 3.48–3.40 (m, 2H, H-5, H-2), 1.99 (s, 3H, CH_3CONH), 1.65–1.58 (m, 1H, $SiC(CH_3)_2CH(CH_3)_2$), 0.88–0.84 (m, 12H, $SiC(CH_3)_2CH(CH_3)_2$), 0.15 (s, 3H, $SiCH_3$), 0.14 (s, 3H, $SiCH_3$); ^{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 satd 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); ^{1}H NMR (400 MHz) δ 7.38 (d, 2H, J = 8.0 Hz, Ar-H), 6.87 (d, 2H, J = 8.0 Hz, Ar-H), 5.93 (br s, 1H, CH_3CONH), 5.89–5.81 (m, 1H, $CH_2CH{=}CH_2$), 5.46 (s, 1H, $ArCHO_2$), 5.23–5.16 (m, 2H, H-1, $CH_2CH{=}CH_2$), 5.10 (d, 1H, J = 10.4 Hz, $CH_2CH{=}CH_2$), 4.31 (dd, 1H, J = 5.6, 13.2 Hz, $CH_2CH{=}CH_2$), 4.24 (dd, 1H, J = 4.8, 10.8 Hz, H-6_a), 4.14–4.07 (m,

2H, $CH_2CH{=}CH_2$, H-3), 3.78 (s, 3H, OCH_3), 3.72 (t, 1H, J = 10.6 Hz, H-6_b), 3.58 (t, 1H, J = 9.0 Hz, H-4), 3.50–3.44 (m, 1H, H-5), 3.24–3.21 (m, 1H, H-2), 1.95 (s, 3H, CH_3CONH), 1.62–1.57 (m, 1H, $SiC(CH_3)_2CH(CH_3)_2$), 0.86 (s, 3H, $SiC(CH_3)_2CH(CH_3)_2$), 0.85 (s, 3H, $SiC(CH_3)_2CH(CH_3)_2$), 0.83 (s, 6H, $SiC(CH_3)_2CH(CH_3)_2$), 0.13 (s, 3H, $SiCH_3$), 0.12 (s, 3H, $SiCH_3$); ^{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 anhyd 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 × 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); ^{1}H NMR (400 MHz) δ 7.23 (d, 2H, J = 8.0 Hz, Ar-H), 6.85 (d, 1H, J = 8.8 Hz, Ar-H), 5.92–5.83 (m, 1H, $CH_2CH{=}CH_2$), 5.72 (d, 1H, J = 7.2 Hz, CH_3CONH), 5.24 (d, 1H, J = 17.2 Hz, $CH_2CH{=}CH_2$), 5.13 (d, 1H, J = 9.6 Hz, $CH_2CH{=}CH_2$), 5.02 (d, 1H, J = 7.2 Hz, H-1), 4.53–4.46 (m, 2H, $ArCH_2O$), 4.24 (dd, 1H, J = 5.6, 13.2 Hz, $CH_2CH{=}CH_2$), 4.15 (dd, 1H, J = 6.0, 13.2 Hz, $CH_2CH{=}CH_2$), 3.85 (t, 1H, J = 10.0 Hz, H-3), 3.79 (s, 3H, OCH_3), 3.69 (d, 2H, J = 4.8 Hz, H-6_a, H-6_b), 3.56 (t, 1H, J = 8.8 Hz, H-4), 3.51–3.46 (m, 1H, H-5), 3.25–3.20 (m, 1H, H-2), 3.08 (br s, 1H, OH), 1.94 (s, 3H, CH_3CONH), 1.63–1.56 (m, 1H, $SiC(CH_3)_2CH(CH_3)_2$), 0.86 (s, 3H, $SiC(CH_3)_2CH(CH_3)_2$), 0.84 (s, 3H $SiC(CH_3)_2CH(CH_3)_2$), 0.82 (s, 6H, $SiC(CH_3)_2CH(CH_3)_2$), 0.14 (s, 3H, $SiCH_3$), 0.11 (s, 3H, $SiCH_3$); ^{13}C NMR (100 MHz) δ 170.4, 159.5, 135.4, 130.2, 129.5, 117.2, 114.0, 95.2, 80.6, 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); ^{1}H NMR (500 MHz) δ 7.23 (d, 2H, J = 8.5 Hz, Ar-H), 6.85 (d, 1H, J = 8.0 Hz, Ar-H), 5.92–5.86 (m, 1H, $CH_2CH{=}CH_2$), 5.84 (d, 1H, J = 8.5 Hz, CH_3CONH), 5.24 (d, 1H, J = 17.0 Hz, $CH_2CH{=}CH_2$), 5.14 (d, 1H, J = 10.5 Hz, $CH_2CH{=}CH_2$), 5.02 (d, 1H, J = 7.5 Hz, H-1), 4.73 (d, 1H, J = 10.5 Hz, $ArCH_2O$), 4.54 (d, 1H, J = 11.0 Hz, $ArCH_2O$), 4.28 (dd, 1H, J = 5.0, 12.5 Hz, $CH_2CH{=}CH_2$), 4.14 (dd, 1H, J = 6.0, 13.0 Hz, $CH_2CH{=}CH_2$), 3.93 (t, 1H, J = 10.0 Hz, H-3), 3.78 (s, 4H, OCH_3, H-6_a), 3.64–3.62 (m, 1H, H-6_b), 3.45 (t, 1H, J = 9.5 Hz, H-4), 3.42–3.38 (m, 1H, H-5), 3.30–3.25 (m, 1H, H-2), 1.98 (s, 3H, CH_3CONH), 1.63–1.56 (m, 1H, $SiC(CH_3)_2CH(CH_3)_2$), 0.86 (s, 3H, $SiC(CH_3)_2CH(CH_3)_2$), 0.84 (s, 3H, $SiC(CH_3)_2CH(CH_3)_2$), 0.82 (s, 6H, $SiC(CH_3)_2CH(CH_3)_2$), 0.14 (s, 3H, $SiCH_3$), 0.10 (s, 3H, $SiCH_3$); ^{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 $C_{27}H_{45}NO_7SiNa$ [M + 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 mixture 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 aq $NaHCO_3$, 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); ^{1}H NMR (500 MHz) δ 7.22 (d, 2H, J = 8.5 Hz, Ar-H), 6.84 (d, 2H, J = 9.0 Hz, Ar-H), 5.82–5.74 (m, 2H, CH_3CONH, $CH_2CH{=}CH_2$), 5.21–5.15 (m, 2H, H-1, $CH_2CH{=}CH_2$), 5.10 (dd, 1H, J = 1.5, 10.5 Hz, $CH_2CH{=}CH_2$), 4.89 (t, 1H, J = 9.5 Hz, H-4), 4.43 (s, 2H, Ar-CH_2), 4.17 (t, 1H, J = 9.5 Hz, H-3), 4.06–4.04 (m, 2H, $CH_2CH{=}CH_2$), 3.78 (s, 3H, OCH_3), 3.63–3.59 (m, 1H, H-5), 3.49–3.48 (m, 2H, H-6_a, H-6_b), 3.14–3.09 (m, 1H, H-2), 1.96 (s, 3H, CH_3COO), 1.94 (s, 3H, CH_3CONH), 1.64–1.58 (m, 1H, $SiC(CH_3)_2CH(CH_3)_2$), 0.86 (d, 3H, J = 2.0 Hz, $SiC(CH_3)_2CH(CH_3)_2$), 0.85 (d, 3H, J = 2.0 Hz, $SiC(CH_3)_2CH(CH_3)_2$), 0.83 (s, 3H, $SiC(CH_3)_2CH(CH_3)_2$), 0.82 (s, 3H, $SiC(CH_3)_2CH(CH_3)_2$), 0.16 (s, 3H, $SiCH_3$), 0.12 (s, 3H, $SiCH_3$); ^{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 $C_{29}H_{47}NO_8SiNa$ [M + 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); ^{1}H NMR (500 MHz) δ 7.22 (d, 2H, J = 8.5 Hz, Ar-H), 6.85 (d, 2H, J = 8.5 Hz, Ar-H), 5.94–5.86 (m, 1H, $CH_2CH{=}CH_2$), 5.80–5.76 (m, 1H, CH_3CONH), 5.25 (dd, 1H, J = 1.5, 17.5 Hz, $CH_2CH{=}CH_2$), 5.14 (d, 1H, J = 10.5 Hz, $CH_2CH{=}CH_2$), 4.97 (d, 1H, J = 8.0 Hz, H-1), 4.73 (d, 1H, J = 10.5 Hz, Ar-CH_2), 4.48 (d, 1H, J = 10.5 Hz, $ArCH_2$), 4.30–4.25 (m, 2H, $CH_2CH{=}CH_2$, H-6_a), 4.17–4.10 (m, 2H, $CH_2CH{=}CH_2$, H-6_b), 3.95 (t, 1H, J = 9.5 Hz, H-3), 3.78 (s, 3H, OCH_3), 3.54–3.51 (m, 1H, H-5), 3.38 (t, 1H, J = 9.0 Hz, H-4), 3.31–3.26 (m, 1H, H-2), 2.01 (s, 3 H, CH_3COO), 1.94 (s, 3H, CH_3CONH), 1.61–1.56 (m, 1H, $SiC(CH_3)_2CH(CH_3)_2$), 0.85 (d, 3H, J = 1.5 Hz, $SiC(CH_3)_2CH(CH_3)_2$), 0.83 (d, 3H, 1.0 Hz, $SiC(CH_3)_2CH(CH_3)_2$), 0.81 (s, 3H, $SiC(CH_3)_2CH(CH_3)_2$), 0.80 (s, 3H, $SiC(CH_3)_2CH(CH_3)_2$), 0.11 (s, 3H, $SiCH_3$), 0.10 (s, 3H, $SiCH_3$); ^{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 $C_{29}H_{47}NO_8SiNa$ [M + Na$^+$]: 588.2969. Found: 588.2967.

1.7. Dimethylthexylsilyl 2-*O*-benzoyl-3,4,6-tri-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2-acetamido-3-*O*-allyl-2-deoxy-6-*O*-(4-methoxybenzyl)-β-D-glucopyranoside (9)

A solution of **4** (253 mg, 483 μmol) in CH_2Cl_2 (15 mL) was stirred for 2 h in the presence of 5 Å MS (820 mg) at ambient temperature under N_2 atmosphere after which TMSOTf (48 μL, 265 μmol) 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 μmol, 51%). $[\alpha]_D^{21}$ +13.1 (c 0.8); ^{1}H NMR (500 MHz) δ 7.97 (d, 2H, J = 7.5 Hz, Ar-H), 7.58 (t, 1H, J = 7.5 Hz, Ar-H), 7.46–7.57 (t, 2H, J = 8.0 Hz, Ar-H), 7.38–7.11 (m, 17H, Ar-H), 6.88 (d, 2H, J = 8.5 Hz, Ar-H), 5.88–5.82 (m, 2H,

CH_3CONH, $CH_2CH{=}CH_2$), 5.24–5.18 (m, 2H, H″-2, $CH_2CH{=}CH_2$), 5.05 (d, 1H, J = 10.5 Hz, $CH_2CH{=}CH_2$), 4.81 (d, 1H, J = 10.5 Hz, $ArCH_2$), 4.76 (d, 1H, J = 6.5 Hz, H′-1), 4.74 (d, 1H, J = 11.5 Hz, $ArCH_2$), 4.66–4.52 (m, 6H, H″-1, $ArCH_2$), 4.31 (d, 1H, J = 11.5 Hz, $ArCH_2$), 4.28 (dd, 1H, J = 5.0, 13.0 Hz, $CH_2CH{=}CH_2$), 4.11 (dd, 1H, J = 5.5, 13.0 Hz, $CH_2CH{=}CH_2$) 3.96 (t, 1H, J = 7.0 Hz, H′-3), 3.83–3.69 (m, 8 H, OCH_3, H′-4, H′-6_a, H′-6_b, H″-6_a, H″-6_b), 3.58–3.53 (m, 3H, H″-3, H″-4, H′-5), 3.46–3.42 (m, 1 H, H″-5), 3.41–3.38 (m, 1H, H′-2), 1.99 (s, 3H, CH_3CONH), 1.59–1.54 (m, 1H, $SiC(CH_3)_2CH(CH_3)_2$), 0.84 (d, 3H, J = 2.5 Hz, $SiC(CH_3)_2CH(CH_3)_2$), 0.82 (d, 3H, J = 2.5 Hz, $SiC(CH_3)_2CH(CH_3)_2$), 0.78 (s, 3H, $SiC(CH_3)_2CH(CH_3)_2$), 0.77 (s, 3H, $SiC(CH_3)_2CH(CH_3)_2$), 0.03 (s, 3H, $SiCH_3$), −0.02 (s, 3H, $SiCH_3$); ^{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 ($C_{1''}$, $J_{C1''-H1''}$ = 163.4), 95.2 ($C_{1'}$, $J_{C1'-H1'}$ = 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 $C_{61}H_{77}NO_{13}SiNa$ [M+Na$^+$]: 1082.5062. Found: 1082.5066.

1.8. Dimethylthexylsilyl 3,4,6-tri-*O*-benzyl-β-D-glucopyranosyl-(1→4)-2-acetamido-3-*O*-allyl-2-deoxy-6-*O*-(4-methoxybenzyl)-β-D-glucopyranoside (10)

To a solution of **9** (160.0 mg, 151 μmol) in MeOH–THF (1:1, v:v, 6 mL) was added a solution of NaOMe in MeOH (25 wt %, 150 μL, 656 μmol). 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 mixture 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 μmol, 77%). $[\alpha]_D^{21}$ +17.5 (c 1.3); ^1H NMR (500 MHz) δ 7.39–7.27 (m, 15H, Ar-H), 7.17 (d, 2H, J = 7.5 Hz, Ar-H), 6.87 (d, 2H, J = 9.0 Hz, Ar-H), 5.88–5.81 (m, 1H, $CH_2CH{=}CH_2$), 5.75 (d, 1H, J = 7.5 Hz, CH_3CONH), 5.19 (d, 1H, J = 12.5 Hz, $CH_2CH{=}CH_2$), 5.06–5.03 (m, 2H, $CH_2CH{=}CH_2$, H′-1), 4.94 (d, 1H, J = 11.5 Hz, $ArCH_2$), 4.84–4.80 (m, 2H, $ArCH_2$), 4.62 (d, 1H, J = 12.0 Hz, $ArCH_2$), 4.58–4.47 (m, 5H, $ArCH_2$, H″-1), 4.45 (dd, 1H, J = 5.0, 12.5 Hz, $CH_2CH{=}CH_2$), 4.08–4.02 (m, 2H, $CH_2CH{=}CH_2$, H′-3), 3.96–3.91 (m, 2H, H′-4, H′-6_a), 3.76 (s, 3H, OCH_3), 3.70–3.66 (m, 3H, H′-6_b, H″-6_a, H″-6_b), 3.63–3.59 (m, 2H, H″-4, OH), 3.52–3.45 (m, 3H, H″-2, H″-3, H′-5), 3.42–3.39 (m, 1H, H″-5), 3.25–3.20 (m, 1H, H′-2), 1.94 (s, 3H, CH_3CONH), 1.65–160 (m, 1H, $SiC(CH_3)_2CH(CH_3)_2$), 0.88 (d, 3H, J = 2.5 Hz, $SiC(CH_3)_2CH(CH_3)_2$), 0.87 (d, 3H, J = 2.5 Hz, $SiC(CH_3)_2CH(CH_3)_2$), 0.84 (s, 3H, $SiC(CH_3)_2CH(CH_3)_2$), 0.83 (s, 3H, $SiC(CH_3)_2CH(CH_3)_2$), 0.16 (s, 3H, $SiCH_3$), 0.12 (s, 3H, $SiCH_3$); ^{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 ($C_{1''}$, $J_{C1''-H1''}$ = 165.7), 95.0 ($C_{1'}$, $J_{C1'-H1'}$ = 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 $C_{54}H_{73}NO_{12}SiNa$ [M + Na$^+$]: 978.4800. Found: 978.4823.

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

To a solution of **10** (110.5 mg, 116 μmol) in CH_2Cl_2 (6 mL) was added Dess–Martin periodinane (97 mg, 229 μmol). 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 satd aq $NaHCO_3$ containing $Na_2S_2O_3$ and brine. The organic phase was dried over Na_2SO_4 and concentrated. The resulting residue was dissolved in MeOH–CH_2Cl_2 (1:1, v:v, 6 mL). The solution was cooled to 0 °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 mixture 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 μmol, 84%) and **10** (5.0 mg, 5.2 μmol, 4.5%).

Compound **11**: $[\alpha]_D^{21}$ +2.8 (c 1.0); ^1H NMR (500 MHz) δ 7.36–7.20 (m, 17H, Ar-H), 6.85 (d, 2H, J = 8.5 Hz, Ar-H), 5.94 (d, 1H, J = 8.0 Hz, CH_3CONH), 5.87–5.81 (m, 1H, $CH_2{=}CHCH_2$), 5.19 (d, 1H, J = 12.5 Hz, $CH_2{=}CHCH_2$), 5.05 (d, 1H, J = 10.0 Hz, $CH_2{=}CHCH_2$), 5.02 (d, 1H, J = 6.5 Hz, H′-1), 4.86 (d, 1H, J = 11.0 Hz, $ArCH_2$), 4.67 (d, 1H, J = 12.0 Hz, $ArCH_2$), 4.61 (s, 1H, H″-1), 4.58–4.51 (m, 5H, $ArCH_2$), 4.43 (d, 1H, J = 11.5 Hz, $ArCH_2$), 4.28 (dd, 1H, J = 5.5, 12.5 Hz, $CH_2{=}CHCH_2$), 4.10 (dd, 1H, J = 6.0, 12.5 Hz, $CH_2{=}CHCH_2$), 4.03 (d, 1H, J = 3.0 Hz, H″-2), 3.99 (t, 1H, J = 8.0 Hz, H′-3), 3.93 (t, 1H, J = 8.0 Hz, H′-4), 3.87 (t, 1H, J = 9.5 Hz, H″-4), 3.77–3.69 (m, 7H, OCH_3, H′-6_a, H′-6_b, H″-6_a, H″-6_b), 3.60–3.57 (m, 1H, H′-5), 3.47–3.42 (m, 2H, H′-2, H″-3), 3.36–3.33 (m, 1H, H″-5), 2.60 (br s, 1H, OH), 1.94 (s, 3H, CH_3CONH), 1.66–1.60 (m, 1H, $SiC(CH_3)_2CH(CH_3)_2$), 0.87 (d, 3H, J = 2.5 Hz, $SiC(CH_3)_2CH(CH_3)_2$), 0.86 (d, 3H, J = 2.5 Hz, $SiC(CH_3)_2CH(CH_3)_2$), 0.84 (s, 6H, $SiC(CH_3)_2CH(CH_3)_2$), 0.15 (s, 3H, $SiCH_3$), 0.13 (s, 3H, $SiCH_3$); ^{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 ($C_{1''}$, $J_{C1''-H1''}$ = 160.6), 95.0 ($C_{1'}$, $J_{C1'-H1'}$ = 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 $C_{54}H_{73}NO_{12}SiNa$ [M + Na$^+$]: 978.4800. Found: 978.4818.

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

To a solution of **11** (89.0 mg, 93 μmol) in pyridine (2 mL) was added benzylsulfonyl chloride (31.0 mg, 162 μmol) at 0 °C under N_2 atmosphere. After stirring 7 h, TLC (EtOAc–hexane 1:1) showed that the reaction went to completion. The reaction mixture was diluted with CH_2Cl_2, washed with 0.1 N HCl, satd aq $NaHCO_3$, 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 μmol, 97%) as a syrup. $[\alpha]_D^{22}$ −43.6 (c 0.8); ^1H NMR (500 MHz) δ 7.42–7.26 (m, 22H, Ar-H), 6.85 (d, 2H, J = 9.0 Hz, Ar-H), 5.93 (d, 1H, J = 8.5 Hz, CH_3CONH), 5.84–5.78 (m, 1H, $CH_2{=}CHCH_2$), 5.17 (d, 1H, J = 17.0 Hz, $CH_2{=}CHCH_2$), 5.11 (d, 1H, J = 2.0 Hz, H″-2), 5.03 (d, 1H, J = 10.5 Hz, $CH_2{=}CHCH_2$), 4.93 (d, 1H, J = 7.5 Hz, H′-1), 4.90 (d, 1H, J = 10.5 Hz, $ArCH_2$), 4.76 (d, 1H, J = 11.0 Hz, $ArCH_2$), 4.63–4.49 (m, 6H, $ArCH_2$, H″-1), 4.43 (d, 1H, J = 12.0 Hz, $ArCH_2$), 4.38 (s, 2H, $ArCH_2SO_2$), 4.22 (dd, 1H, J = 5.0, 13.0 Hz, $CH_2{=}CHCH_2$), 4.13 (dd, 1H, J = 5.5, 13.0 Hz, $CH_2{=}CHCH_2$), 3.97 (t, 1H, J = 6.0 Hz, H′-3), 3.81–3.65 (m, 11H, 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, 1H, J = 3.0, 9.5 Hz, H″-3), 3.34–3.32 (m, 1H, H″-5) 1.80 (s, 3H, CH_3CONH), 1.64–1.60 (m, 1H, $SiC(CH_3)_2CH(CH_3)_2$), 0.88–0.84 (m, 12H, $SiC(CH_3)_2CH(CH_3)_2$), 0.15 (s, 3H, $SiCH_3$), 0.14 (s, 3H, $SiCH_3$); ^{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 ($C_{1''}$, $J_{C1''-H1''}$ = 160.4), 95.3 ($C_{1'}$, $J_{C1'-H1'}$ = 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 $C_{61}H_{79}NO_{14}SiNa$ [M+Na$^+$]: 1132.4888. Found: 1132.4905.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2008.10.007.

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