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Unexpected α-stereochemical outcomes of attempted β-glycosylations

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Abstract

In an effort to prepare complex oligosaccharide derivatives, a series of unexpected α glycosides were predominantly formed in the presence of neighboring group participation using imidates or thioglycosides as glycosyl donors under standard glycosylation conditions. The observations are especially suitable in the case of α-(1→3) glycosidic bond formation.

Keywords: Neighboring group participation effects; Stereoselectivity; Glycosylation; Oligosaccharide

1. Introduction

The stereoselective formation of a glycosidic bond is one of the most challenging aspects of oligosaccharide synthesis. Now it is well known that the presence of an acyl protection group on O-2 of a glycosyl donor commonly induces the exclusive formation of a 1,2-trans glycoside because of the neighboring group participation effect.[1] Although this principle has provided much empirical knowledge in the design of glycosylation reagents, organic chemists are still confused with carbohydrate coupling reactions that proceed in low yields and give poor β/α ratios. Although factors that may affect the glycosylation results have been extensively studied, one still can be misled when playing a real glycosylation strategy.[2] In our previous project on the synthesis of sanqi hexasaccharide,[3] an active component of Chinese herbal medicine derived from *Panax notoginseng*, we obtained an unexpected α-product predominantly using an O-2 acetylated donor via a [3 + 3] strategy. This intriguing result promoted us to put more effort into researching this issue, and we found that this phenomenon is to some extent a general one. We now report our observations in complex carbohydrate coupling reactions with unexpected α stereoselectivity in the presence of neighboring group participation.

2. Results and discussion

Glycosylation of 2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl-(1→3)-1,2-*O*-ethylidene-α-D-galactopyranose[3] (**1**) and 2.2 equivalents of 2,3,5-tri-*O*-benzoyl-α-L-arabinofuranosyl trichloroacetimidate[4] (**2**) in dry CH_2Cl_2 with TMSOTf as promoter afforded 2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl-(1→3)-[4,6-di-*O*-(2,3,5-tri-*O*-benzoyl-α-L-arabinofuranosyl)]-1,2-*O*-ethylidene-α-D-galactopyranose (**3**, 74.6%). Removal of the 1,2-*O*-ethylidene group[5] in aqueous 95% TFA, followed by acetylation in pyridine, regioselective deacetylation[6] on the anomeric carbon, and Schmidt activation,[7] afforded 2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl-(1→3)-[4,6-di-*O*-(2,3,5-tri-*O*-benzoyl-α-L-arabinofuranosyl)]-2-*O*-acetyl-α-D-galactopyranosyl trichloroacetimidate (**4**) in a total yield of 68% (from **3**, Scheme 1). Coupling of tetrasaccharide donor **4** and trisaccharide acceptor **5**[3] in dry CH_2Cl_2 at −20 °C gave α products **6** [(1→4 linkage, 55%) and **7** (1→3 linkage, 20%)]. We have run ^1H NMR, coupled ^{13}C NMR and ^1H–^1H, ^1H–^{13}C COSY experiments to secure the assignments of these two compounds. In **6**, the

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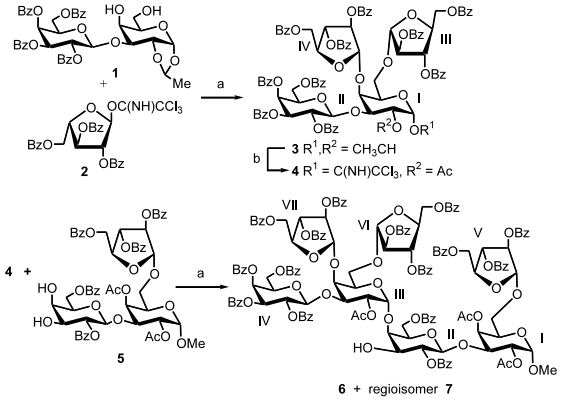
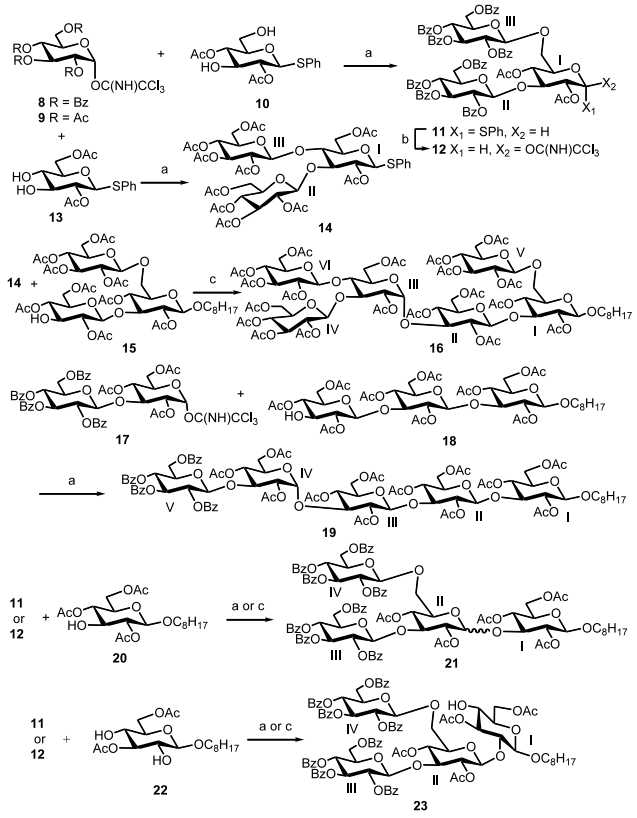
H-1^{III} of sugar residue III appears at δ 5.15 ppm ($J_{1,2} < 1$ Hz) in the ^{1}H NMR spectrum, while the corresponding C-1^{III} at δ 98.9 ppm ($J_{C\text{-}1,\ H\text{-}1}$ 174 Hz) in the ^{13}C NMR spectrum indicated an α linkage between carbohydrate units II and III. Compared to acceptor **5**, the chemical shift of C-4^{II} in **6** moves downfield to δ 79.2 ppm from δ 68.8 ppm, while the C-3^{II}s of **5** and **6**



Scheme 1. Reagents and conditions: (a) TMSOTf, CH_2Cl_2; 74.6% for **3**; 55% for **6**, 20% for **7**; (b) 95% TFA; Ac_2O, Pyr; NH_3, 3:7 MeOH–THF; Cl_3CCN, DBU; 68% for four steps.



Scheme 2. Reagents and conditions: (a) TMSOTf, CH_2Cl_2; 79% for **11**; 82% for **14**; 77% for **19**; 70% for **21** (α:β = 1:2.3); 85% for **23**; (b) NBS, CH_2Cl_2, H_2O; Cl_3CCN, DBU; 71% for two steps; (c) NIS, TMSOTf; 62% for **21** (α:β = 1:2); 73% for **23**.

appear at δ 72.2 ppm and δ 71.9 ppm in the ^{13}C NMR spectra, respectively, which confirmed the C-4 glycosylation of unit II. Similarly, H-1^{III} of compound **7** appears at δ 4.81 ppm ($J_{1,2}$ 3.0 Hz) in the ^{1}H NMR spectrum and C-1^{III} at δ 96.77 ppm ($J_{C\text{-}1,\ H\text{-}1}$ 172 Hz) in the ^{13}C NMR spectrum, both of which correspond to the newly formed α glycosidic bond between sugar units II and III. The 1→3 linkage of **7** was confirmed later by its fully acetylated derivative. No β components were isolated in our experiments.

This observation of preferred α bond formation was further supported by the results in our project of (1→3)-linked β-glucan preparation (Scheme 2). Trisaccharide thioglycoside donors **11** and **14** were synthesized according to our previous method.[8,9] Treatment of **11** with NBS, followed by Schmidt activation[7] gave imidate **12** in a total yield of 71%. Condensation of 3,4-branched trisaccharide thioglycoside **14** with 3^{II}-OH trisaccharide acceptor **15**[8] in dry CH_2Cl_2 in the presence of NIS and TMSOTf gave the α product **16** at 0 °C in 56% isolated yield. C-1^{III} at δ 95.5 ppm in the ^{13}C NMR spectrum clearly indicated the newly formed α glycosidic bond in **16**. More frustration was met in the attempted preparation of β-(1→3)-linked linear pentaglucopyranoside. Coupling of the disaccharide imidate **17** with the trisaccharide acceptor **18**,[10] as described in the preparation of **6**, gave α-(1→3)-linked pentasaccharide **19** in 77% yield. H-1^{IV} and C-1^{IV} appear at δ 5.11 and 95.2 ppm in ^{1}H and ^{13}C NMR spectra, respectively, to support our conjecture.

Interestingly, when 3,6-branched trisaccharide donor **11** or **12** was coupled with 3-OH monosaccharide acceptor **20** under standard glycosylation conditions, an inseparable α,β mixture **21** was obtained in 62–70% yield in a ratio of 1:2 (α:β). Under the same reaction conditions, condensation of **11** or **12** with 2,4-diol **22** gave exclusively β-(1→2)-coupled product **23** in high yield (85%, H-1^{II} appears at δ 4.55 ppm, $J_{1,2}$ 7.8 Hz).

In conclusion, we have observed that α or β glycosidic bond formation is strongly dependent on the properties of glycosyl donor and acceptor. The stereochemical outcome of the coupling reaction (α:β ratio) may be determined by the transition state of the glycosylation couples, such as orthoester and oxocarbonium ion.[11] β-(1→6)-linked bonds have been prepared smoothly under standard glycosylation conditions using [3 + 3] strategy.[12] We then believe that the bulky acceptor, such as a 3-OH acceptor compared to a 6-OH one, disfavors orthoester rearrangement of forming a β glycoside. Instead, an oxocabonium ion, which converted from the orthoester intermediate, becomes more predominant, leading to a high proportion of α products. It is worth noting that from our experiments, neighboring group participation is far from sufficient in these examples to secure β glycosylation in complex oligosaccharide synthesis.

3. Experimental

General methods.—Optical rotations were determined at 20 °C with a Perkin–Elmer Model 241 MC automatic polarimeter. ^{1}H, ^{13}C NMR and ^{1}H–^{1}H, ^{1}H–^{13}C COSY spectra were recorded with ARX 400 spectrometers for solutions in $CDCl_3$. Chemical shifts are given in ppm downfield from internal Me_4Si. Mass spectra were measured using MALDITOF-MS with α-cyano-4-hydroxycinnamic acid (CCA) as the matrix. High-resolution thin-layer chromatography (HRTLC) was performed on silica gel HF_{254} with detection by charring with 30% (v/v) H_2SO_4 in MeOH or in some cases by UV detection. Column chromatography was conducted by elution of a column (10 × 200 mm, 18 × 300 mm, 35 × 400 mm) of silica gel (100–200 mesh) with EtOAc–petroleum ether (bp 60–90 °C) as the eluent. Solutions were concentrated at < 60 °C under diminished pressure.

2,3,4,6-Tetra-O-*benzoyl*-β-D-*galactopyranosyl*-(1→3)-[*4,6-di*-O-(*2,3,5-tri*-O-*benzoyl*-α-L-*arabinofuranosyl*)]-*1,2*-O-*ethylidene*-α-D-*galactopyranose* (**3**). To a solution of **1** (1.15 g, 1.47 mmol) and **2** (1.96 g, 3.23 mmol) in CH_2Cl_2 (20 mL) at 0 °C were added TMSOTf (40 μL, 0.22 mmol) under a N_2 atmosphere. The mixture was stirred at this temperature for 1.5 h, at which time TLC indicated the reaction was complete. The mixture was then neutralized with Et_3N and concentrated. The residue was subjected to column chromatography on silica gel with 2:1 petroleum ether–EtOAc as the eluent to give **3** (*R*, *S* mixture) as a syrup (1.83 g, 74.6%): ^{1}H NMR (300 MHz, $CDCl_3$): 1.33 (d, 3 H, *J* 4.8 Hz, $CHCH_3$), 3.86–4.01 (m, 4 H), 4.09–4.71 (m, 13 H), 4.97–5.02 (m, 1 H), 5.07 (d, 1 H, *J* 5.1 Hz), 5.25–5.75 (m, 6 H), 5.96 (d, 1 H, *J* 3.3 Hz), 5.99 (s, 1 H), 7.14–8.09 (m, 50 H, PhCO). Anal. Calcd for $C_{94}H_{80}O_{29}$: C, 67.46; H, 4.82. Found: C, 67.37; H, 4.75.

2,3,4,6-Tetra-O-*benzoyl*-β-D-*galactopyranosyl*-(1→3)-[*4,6-di*-O-(*2,3,5-tri*-O-*benzoyl*-α-L-*arabinofuranosyl*)]-*2*-O-*acetyl*-α-D-*galactopyranosyl trichloroacetimidate* (**4**). To a solution of **3** (1.72 g, 1.03 mmol) in CH_2Cl_2 (4 mL) was added aq 95% TFA (15 mL). The mixture was stirred at rt for 4 h, then co-evaporated with toluene under reduced pressure. The residue was dissolved in pyridine (12 mL) and Ac_2O (5 mL), stirred at rt for 6 h, then concentrated to dryness. Part of the above residue (0.93 g, 0.54 mmol) in ammonia saturated 7:3 THF–MeOH (100 mL) was stirred at rt for 50 min, then the solvents were evaporated at 40 °C. The residue was subjected to column chromatography on silica gel with 3:2 petroleum ether–EtOAc as the eluent. The pure intermediate (0.74 g, 0.43 mmol) was dissolved in CH_2Cl_2 (6 mL), then CCl_3CN (0.3 mL, 3 mmol) and DBU (30 μL) were added at 0 °C. The mixture was stirred at rt for 2 h, then concentrated. The residue was subjected to column chromatography on silica gel with 3:2 petroleum ether–EtOAc as eluent to give **4** as a syrup (1.29 g, 68% for four steps): $[\alpha]_D$ +36° (*c* 1, $CHCl_3$); ^{1}H NMR: 1.60 (s, 3 H, $COCH_3$), 3.97 (d, 1 H, *J* 4.6 Hz, H-4^I), 4.30–4.34 (m, 2 H, H-3^I and H-5^I), 4.37–4.50 (m, 3 H, H-4^{III}, 2 H-6^I), 4.61 (dd, 2 H, *J* 11.6, 4.2 Hz, 2 H-5^{III}), 4.65–4.73 (m, 5 H, H-4^{IV}, H-5 ^{II}, H-6a^{II}, 2 H-5^{IV}), 4.78 (dd, 1 H, *J* 11.8, 4.3 Hz, H-6b^{II}), 5.10 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1^{II}), 5.21 (s, 1 H, H-1^{III}), 5.32 (dd, 1 H, *J* 10.4, 3.6 Hz, H-2^I), 5.45 (d, 1 H, *J* 0.8 Hz, H-2^{III}), 5.50 (d, 1 H, *J* 5.1 Hz, H-3^{III}), 5.58–5.62 (m, 2 H, H-3^{II} and H-3^{IV}), 5.72 (dd, 1 H, *J* 10.4, 7.8 Hz, H-2^{II}), 5.73 (s, 1 H, H-2^{IV}), 5.95 (d, 1 H, *J* 3.4 Hz, H-4^{II}), 6.25 (s, 1 H, H-1^{IV}), 6.53 (d, 1 H, *J* 3.6 Hz, H-1^I), 7.06–8.14 (m, 50 H, Ph), 8.46 (s, 1 H, =NH); MALDITOF-MS Calcd for $C_{96}H_{80}Cl_3NO_{30}$: 1831.38 [M]. Found: 1854.3 $[M + Na]^+$.

Methyl 2,3,4,6-tetra-O-*benzoyl*-β-D-*galactopyranosyl*-(1→3)-[*4,6-di*-O-(*2,3,5-tri*-O-*benzoyl*-α-L-*arabinofuranosyl*)]-*2*-O-*acetyl*-α-D-*galactopyranosyl*-(1→4)-*2,6-di*-O-*benzoyl*-β-D-*galactopyranosyl*-(1→3)-[*2,3,5-tri*-O-*benzoyl*-α-L-*arabinofuranosyl*-(1→6)]-*2*-O-*acetyl*-α-D-*galactopyranoside* (**6**). To a mixture of **4** (570 mg, 0.31 mmol) and **5** (328 mg, 0.30 mmol) in dry CH_2Cl_2 (5 mL) at −20 °C was added TMSOTf (10 μL, 0.055 mmol). The mixture was stirred at this temperature for 2 h, at which time TLC indicated the reaction was complete. The mixture was neutralized with Et_3N and concentrated. The residue was subjected to column chromatography on silica gel with 1:1 petroleum ether–EtOAc as the eluent to give syrupy **6** (0.46 g, 55%) and its α-(1→3)-linked regioisomer **7** (0.17 g, 20%). For **6**: $[\alpha]_D$ +50° (*c* 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): 1.57 (s, 3 H, $COCH_3$), 1.58 (s, 3 H, $COCH_3$), 2.13 (s, 3 H, $COCH_3$), 3.29 (s, 3 H, OCH_3), 3.64 (dd, 1 H, *J* 8.8, 7.2 Hz, H-6a^I), 3.75 (br d, 1 H, *J* 8.8 Hz, H-5^I), 3.78–3.86 (m, 3 H, H-3^{II}, H-6b^I, H-5^{III}), 3.96 (d, 1 H, *J* 2.4 Hz, H-4^{II}), 4.02 (br d, 1 H, *J* 9.0 Hz, H-6a^{III}), 4.08 (ddd, 1 H, *J* 9.3, 4.4, 1.2 Hz, H-5^{II}), 4.15–4.23 (m, 2 H, H-4^{III}, H-6a^{II}), 4.29 (dd, 1 H, *J* 13.0, 3.6 Hz, H-6b^{III}), 4.41 (dd, 1 H, *J* 3.5, 8.5 Hz, H-3^I), 4.44–4.60 (m, 4 H, H-3^{III}, H-4^V, H-4^{VI}, H-4^{VII}), 4.60 (dd, 1 H, *J* 2.0, 12.0 Hz, H-5a^{VII}), 4.63–4.71 (m, 5 H, H-1^{II}, H-5^{IV}, H-6a^{IV}, H-5a^V, H-5a^{VI}), 4.74–4.82 (m, 5 H, H-5b^{VII}, H-5b^V, H-6b^{II}, H-6b^{IV}, H-5b^{VI}), 4.89 (d, 1 H, *J* 3.6 Hz, H-1^I), 4.99 (dd, 1 H, *J* 8.0, 3.6 Hz, H-2^I), 5.08 (s, 1 H, H-1^{VI}), 5.15 (br s, 1 H, H-1^{III}), 5.25–5.34 (m, 4 H, H-2^{II}, H-1^{IV}, H-2^{VII}, H-2^{III}), 5.42 (d, 1 H, *J* 3.5 Hz, H-3^{VI}), 5.50–5.58 (m, 4 H, H-3^V, H-2^V, H-1^V, H-3^{VI}), 5.60 (d, 1 H, *J* 3.6 Hz, H-4^I), 5.68 (dd, 1 H, *J* 7.6, 3.6 Hz, H-3^{IV}), 5.72–5.78 (m, 2 H, *J* 7.6, 6.4 Hz, H-2^{VI}, H-2^{IV}), 6.02 (d, 1 H, *J* 3.6 Hz, H-4^{IV}), 6.32 (s, 1 H, H-1^{VII}), 7.03–8.07 (m, 75 H, Ph); ^{13}C NMR (125 MHz, $CDCl_3$): 20.04 ($COCH_3$), 20.18 ($COCH_3$), 20.96 ($COCH_3$), 55.18 (OCH_3), 60.34 (C-5^{VI}), 61.30 (C-6^{II}), 61.64 (C-6^{IV}), 63.09 (C-5^V), 63.52 (C-5^V), 64.44 (C-5^{III}), 66.81 (C-6^{III}), 67.86 (C-4^{IV}), 68.91 (C-5^I), 69.78 (C-5^{III}), 70.12, 70.27, 70.42 (3 C), 70.59

(C-4^{I}), 71.12, 71.33, 71.57 (C-5^{II}), 71.93 (C-3^{II}), 72.45 (C-2^{II}), 73.31 (C-3^{I}), 74.62, 75.57 (2 C), 77.25, 77.70 (C-3^{VI}), 77.88 (C-3^{VII}), 79.22 (C-4^{II}), 80.42 (C-4^{V}), 81.26 (C-4^{VI}), 81.62 (C-4^{VII}), 81.83 (C-2^{V}), 82.43 (C-2^{VI}), 82.74 (C-2^{VII}), 96.77 (C-1^{I}), 98.93 (C-1^{III}), 101.74 (C-1^{IV}), 102.37 (C-1^{II}), 105.79 (C-1^{VI}), 106.18 (C-1^{V}), 106.86 (C-1^{VII}), 132.65, 132.75, 132.91, 133.02, 133.17, 133.29, 133.38, 133.47, 133.51, 164.38, 165.23, 165.29, 165.34, 165.39, 165.43, 165.60, 165.63, 165.67, 165.88, 165.95, 166.16, 166.19 (PhCO), 169.87, 170.19, 170.27 (3 CH_3CO). Anal. Calcd for $C_{151}H_{134}O_{51}$: C, 65.60; H, 4.89. Found: C, 65.77; H, 5.01. For **7**: $[\alpha]_D$ +12° (*c* 1, $CHCl_3$); selected ^{1}H NMR (500 MHz, $CDCl_3$): 4.81 (d, 1 H, $J_{1,2}$ 3.0 Hz, H-1^{III}), 4.82 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1^{II}), 4.99 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1^{IV}), 5.13 (s, 1 H, H-1^{V}), 5.28 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1^{I}), 5.32 (s, 1 H, H-1^{VI}), 6.06 (s, 1 H, H-1^{VII}); ^{13}C NMR (125 MHz, $CDCl_3$): 19.98 ($COCH_3$), 20.21 ($COCH_3$), 20.82 ($COCH_3$), 55.03 (OCH_3), 61.07, 61.02, 63.54, 64.15, 64.77, 66.42, 67.60, 68.52, 69.71, 69.78, 70.08, 70.64, 70.84, 71.12, 71.23, 72.05, 72.44, 75.09, 77.66, 77.82, 78.01, 80.23, 80.98, 81.34, 82.03, 82.30, 82.71, 91.66 (C-1^{I}), 96.77 (C-1^{III}), 101.05 (C-1^{II}), 101.81 (C-1^{IV}), 106.19 (C-1^{V} and C-1^{VI}), 106.89 (C-1^{VII}), 128.09–133.74 (Ph), 164.45, 164.92, 165.24 (3 C), 165.43, 165.69 (4 C), 166.04 (3 C), 165.19 (2 C), 169.76, 170.17, 170.30 (CH_3CO-); MALDITOF-MS Calcd for $C_{151}H_{134}O_{51}$: 2762.79 [M]. Found 2785.5 $[M + Na]^+$.

2,3,4,6-Tetra-O-*benzoyl*-*β*-D-*glucopyranosyl*-(1→3)-[*2,3,4,6*-*tetra*-O-*benzoyl*-*β*-D-*glucopyranosyl*-(1→6)]-*2,4*-*di*-O-*acetyl*-*α*-D-*glucopyranosyl trichloroacetimidate* (**12**). To a solution of **11** (3.52 g, 2.32 mmol) in CH_2Cl_2 (20 mL) and H_2O (0.2 mL) was added NBS (476 mg, 2.67 mmol) at rt. TLC indicated the reaction was complete after 4 h. The mixture was washed with aq $Na_2S_2O_3$, then concentrated and subjected to column chromatography on silica gel with 1:1 petroleum ether–EtOAc as the eluent. The pure intermediate was dissolved in CH_2Cl_2 (6 mL), then CCl_3CN (0.8 mL, 8 mmol) and DBU (80 μL) were added at 0 °C. The mixture was stirred at rt for 4 h, then concentrated. The residue was subjected to column chromatography on silica gel with 3:2 petroleum ether–EtOAc as eluent to give **12** as an amorphous solid (2.58 g, 71% for two steps): $[\alpha]_D$ +27° (*c* 1, $CHCl_3$); ^{1}H NMR: 1.79, 1.94 (2 s, 2 × 3 H, $COCH_3$), 3.70 (dd, 1 H, *J* 7.2, 11.7 Hz, H-6a^{I}), 3.93 (dd, 1 H, *J* 1.6, 11.7 Hz, H-6b^{I}), 4.05 (ddd, 1 H, H-5^{I}), 4.10–4.21 (m, 3 H, H-3^{I}, H-5^{II}, H-5^{III}), 4.42 (dd, 1 H, *J* 6.8, 12.1 Hz, H-6a^{II}), 4.48 (dd, 1 H, *J* 6.6, 12.4 Hz, H-6a^{III}), 4.59–4.70 (m, 3 H, H-2^{I}, H-6b^{II}, H-6b^{III}), 4.86 (t, 1 H, $J_{3,4} = J_{4,5} = 9.5$ Hz, H-4^{I}), 4.97 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1^{III}), 4.99 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1^{II}), 5.43 (dd, 1 H, *J* 7.9, 9.7 Hz, H-2^{III}), 5.48 (dd, 1 H, *J* 7.9, 9.7 Hz, H-2^{II}), 5.62 (t, 1 H, *J* 9.7 Hz, H-4^{III}), 5.64 (t, 1 H, *J* 9.7 Hz, H-4^{II}), 5.86 (t, 1 H, *J* 9.7 Hz, H-3^{III}), 5.90 (t, 1 H, *J* 9.7 Hz, H-3^{II}), 6.21 (d, 1 H, *J* 3.6 Hz, H-1^{I}), 7.24–8.02 (m, 40 H, PhCO), 8.34 (s, 1 H, =NH); MALDITOF-MS Calcd for $C_{80}H_{68}Cl_3NO_{26}$: 1563.31 [M]. Found 1586.2 $[M + Na]^+$.

Phenyl 2,3,4,6-tetra-O-*acetyl*-*β*-D-*glucopyranosyl*-(1→3)-[*2,3,4,6*-*tetra*-O-*acetyl*-*β*-D-*glucopyranosyl*-(1→4)]-*2,4*-*di*-O-*acetyl*-*1*-*thio*-*β*-D-*glucopyranoside* (**14**). To a mixture of **9** (2.04 g, 4.14 mmol) and **13** (701 mg, 1.97 mmol) in dry CH_2Cl_2 (10 mL) at 0 °C was added TMSOTf (36 μL, 0.2 mmol). The mixture was stirred at this temperature for 5 h, then neutralized with Et_3N and concentrated. The residue was subjected to column chromatography on silica gel with 1:1 petroleum ether–EtOAc as the eluent to give **14** (1.64 g, 82%): $[\alpha]_D$ −16° (*c* 1, $CHCl_3$); ^{1}H NMR: 1.95, 1.96, 1.99, 2.00, 2.01, 2.02, 2.10, 2.17, 2.22, 2.24 (10 s, 10 × 3 H, $COCH_3$), 3.57 (ddd, *J* 5.5, 11.9, 8.8 Hz, H-5^{I}), 3.60–3.70 (m, 3 H, H-4^{I}, H-5^{II}, H-5^{III}), 3.78 (t, 1 H, *J* 8.8 Hz, H-3^{I}), 4.01 (dd, 1 H, *J* 5.5, 11.9 Hz, H-6a^{I}), 4.12 (dd, 1 H, *J* 1.5, 10.9 Hz, H-6a^{III}), 4.13 (dd, 1 H, *J* 1.2, 11.0 Hz, H-6a^{II}), 4.44 (d, 1 H, *J* 7.9 Hz, H-1^{III}), 4.52 (d, 1 H, *J* 8.0 Hz, H-1^{II}), 4.55 (d, 1 H, *J* 10.1 Hz, H-1^{I}), 4.57 (dd, 1 H, *J* 2.0, 11.9 Hz, H-6a^{I}), 4.63 (dd, 1 H, *J* 3.3, 12.5 Hz, H-6b^{II}), 4.71 (dd, 1 H, *J* 3.3, 12.6 Hz, H-6b^{III}), 4.96 (t, 1 H, *J* 10.1 Hz, H-2^{I}), 5.00 (t, 1 H, *J* 7.9 Hz, H-2^{III}), 5.02 (t, 1 H, *J* 8.0 Hz, H-2^{II}), 5.10–5.21 (m, 4 H, H-3^{II}, H-3^{III}, H-4^{II}, H-4^{III}), 7.26–7.47 (m, 4 H, Ph); Anal. Calcd for $C_{44}H_{56}O_{25}S$: C, 51.97; H, 5.55. Found: C, 52.20; H, 5.48.

Octyl 2,3,4,6-tetra-O-*acetyl*-*β*-D-*glucopyranosyl*-(1→3)-[*2,3,4,6*-*tetra*-O-*acetyl*-*β*-D-*glucopyranosyl*-(1→4)]-*2,6*-*di*-O-*acetyl*-*α*-D-*glucopyranosyl*-(1→3)-*2,4,6*-*tri*-O-*acetyl*-*β*-D-*glucopyranosyl*-(1→3)-[*2,3,4,6*-*tetra*-O-*acetyl*-*β*-D-*glucopyranosyl*-(1→6)]-*2,4*-*di*-O-*acetyl*-*β*-D-*glucopyranoside* (**16**). To a cooled solution (0 °C) of **14** (915 mg, 0.9 mmol) and **15** (845 mg, 0.85 mmol) in anhyd CH_2Cl_2 (4 mL) was added *N*-iodosuccinimide (450 mg, 2 mmol) and TMSOTf (50 μL, 0.28 mmol). The reaction mixture was stirred at 0 °C for 2 h, quenched by Et_3N (two drops), then concentrated. The residue was purified on a silica gel column chromatography to give **16** (905 mg, 56%) as a white foam: $[\alpha]_D$ −12° (*c* 1, $CHCl_3$); ^{1}H NMR: 0.90 (t, 3 H), 1.25–1.30 (m, 10 H), 1.42–1.51 (m, 2 H), 1.94 (s, 3 H), 1.95 (s, 3 H), 1.96 (br s, 6 H), 1.98 (s, 3 H), 1.99 (s, 6 H), 2.01 (s, 9 H), 2.02 (s, 3 H), 2.03 (s, 3 H), 2.08 (s, 3 H), 2.09 (s, 6 H), 2.13 (s, 3 H), 2.14 (s, 3 H), 2.23 (s, 3 H), 2.24 (s, 3 H), 3.40 (dt, 1 H, one proton of OCH_2), 3.49–3.54 (m, 1 H), 3.56–3.91 (m, 12 H), 3.96 (dd, 1 H), 4.05 (dd, 1 H), 4.09–4.40 (m, 3 H), 4.43–4.58 (m, 6 H), 4.62–4.75 (m, 3 H), 4.86–4.94 (m, 2 H), 4.95–5.05 (m, 4 H), 5.10–5.22 (m, 6 H); selected ^{13}C NMR ($CDCl_3$, 100 MHz): 95.48 (C-1^{III}), 99.95 (C-1^{I}), 100.24, 100.38, 100.75, 100.89 (4 C-1), 168.55, 168.73, 168.81, 169.20 (2 C), 169.24, 169.28, 169.39, 169.44 (2 C), 170.13 (2 C), 170.20, 170.24, 170.49, 170.60, 170.63, 171.10, 171.17 (19 CH_3CO); MALDITOF-MS Calcd for $C_{82}H_{116}O_{50}$: 1900.65 [M]. Found: 1923.2 $[M + Na]^+$.

Octyl 2,3,4,6-tetra-O-*benzoyl-β*-D-*glucopyranosyl-(1→3)-2,4,6-tri*-O-*acetyl-α*-D-*glucopyranosyl-(1→3)-2,4,6-tri*-O-*acetyl-β*-D-*glucopyranosyl-(1→3)-2,4,6-tri*-O-*acetyl-β*-D-*glucopyranosyl-(1→3)-2,4,6-tri*-O-*acetyl-β*-D-*glucopyranoside* (**19**). Coupling of **17** (916 mg, 0.89 mmol) and **18** (846 mg, 0.85 mmol) as described in the preparation of **6** gave **19** as a foam (1.22 g, 77%): $[\alpha]_D$ −9° (*c* 8, $CHCl_3$); ^{1}H NMR: 0.88 (t, 3 H, *J* 6.5 Hz, CH_3), 1.24–1.62 (m, 12 H, CH_2), 1.85–2.13 (m, 36 H, 12 $COCH_3$), 3.35–3.43 (m, 1 H, one proton of OCH_2), 3.62–3.70 (m, 2 H, 2 H-5), 3.75–3.90 (m, 6 H), 4.00–4.20 (m, 7 H), 4.23–4.40 (m, 4 H), 4.42–4.55 (m, 3 H), 4.70 (br d, *J* 13 Hz, H-6b^V), 4.83–5.00 (m, 8 H, 4 H-2 and 4 H-4), 5.05 (d, 1 H, *J* 9.6 Hz, H-1^V), 5.11 (br s, 1 H, H-1^{IV}), 5.37 (t, *J* 9.6 Hz, H-2^V), 5.72 (t, 1 H, *J* 9.6 Hz, H-4^V), 5.90 (t, 1 H, *J* 9.6 Hz, H-3^V), 7.25–8.09 (m, 20 H, Ph); selected ^{13}C NMR (100 MHz, $CDCl_3$): 61.41, 61.60, 62.00, 62.20, 62.66, 67.38, 68.35, 69.16, 69.73, 70.07, 71.21, 71.45, 71.68, 71.78, 72.02, 72.40, 72.73, 72.82, 73.04, 73.11, 74.72, 75.72, 77.22, 78.24, 78.51, 95.18 (C-1^{IV}), 100.48 (C-1^I), 100.63 (C-1^{II}), 100.82 (C-1^{III}), 101.13 (C-1^V), 164.95, 164.97, 165.83, 166.00 (4 PhCO), 168.64, 168.66, 168.92, 169.11 (2 C), 169.15, 169.25, 170.03, 170.39, 170.48, 170.55, 170.70 (12 CH_3CO); MALDITOF-MS Calcd for $C_{90}H_{108}O_{42}$: 1860.63 [M]. Found: 1883.6 $[M + Na]^+$.

Octyl 2,3,4,6-tetra-O-*benzoyl-β*-D-*glucopyranosyl-(1→3)-[2,3,4,6-tetra*-O-*benzoyl-β*-D-*glucopyranosyl-(1→6)]-2,4-di*-O-*acetyl-β*-D-*glucopyranosyl-(1→2)-3,6-di*-O-*acetyl-β*-D-*glucopyranoside* (**23**). Method A: Coupling of **11** (520 mg, 0.34 mmol) and **22** (113 mg, 0.3 mmol) as described in the preparation of **16** gave **23** as a syrup (390 mg, 73%). Method B: Coupling of **12** (180 mg, 0.115 mmol) and **22** (41 mg, 0.11 mmol) as described in the preparation of **6** gave **23** in a better yield (166 mg, 85%): $[\alpha]_D$ +18° (*c* 1, $CHCl_3$); ^{1}H NMR: 0.87 (t, 3 H, *J* 6.8 Hz, CH_3), 1.12–1.30 (m, 10 H, 5 CH_2), 1.40–1.48 (m, 2 H, CH_2), 1.85, 1.89, 1.97, 2.00 (4 s, 4 × 3 H, 4 $COCH_3$), 3.17 (s, 1 H, one proton of OCH_2), 3.47–3.53 (m, 4 H, H-6a^{II}, H-5^I, H-5^{II} and one proton of OCH_2), 3.69 (dd, 1 H, *J* 9.3, 7.7 Hz, H-4^I), 3.72 (dd, 1 H, *J* 7.8, 8.5 Hz, H-3^{II}), 3.81 (t, 1 H, *J* 9.3 Hz, H-2^I), 3.85 (dd, 1 H, *J* 12.1, 1.1 Hz, H-6b^{II}), 4.05 (d, 1 H, *J* 7.2 Hz, H-1^I), 4.11 (ddd, 1 H, H-5^{IV}), 4.20 (ddd, 1 H, H-5^{III}), 4.28 (dd, 1 H, *J* 12.6, 2.3 Hz, H-6a^I), 4.36 (dd, 1 H, *J* 12.6, 4.2 Hz, H-6b^I), 4.40–4.50 (m, 2 H, H-6a^{III}, H-6a^{IV}), 4.55 (d, 1 H, *J* 7.8 Hz, H-1^{II}), 4.56–4.61 (m, 2 H, H-6b^{III}, H-6b^{IV}), 4.70 (t, 1 H, *J* 9.3, H-3^I), 4.76 (t, 1 H, *J* 7.8 Hz, H-2^{II}), 4.79 (t, 1 H, *J* 7.8 Hz, H-4^{II}), 4.87 (d, 1 H, *J* 7.8 Hz, H-1^{IV}), 5.20 (d, 1 H, *J* 8.0 Hz, H-1^{III}), 5.39 (dd, 1 H, *J* 9.6, 7.8 Hz, H-2^{IV}), 5.44 (dd, 1 H, *J* 9.6, 8.0 Hz, H-2^{III}), 5.65 (t, 2 H, *J* 9.6 Hz, H-4^{III} and H-4^{IV}), 5.87 (t, 2 H, *J* 9.6 Hz, H-3^{III} and H-3^{IV}), 7.25–8.02 (m, 40 H, PhCO); MALDITOF-MS Calcd for $C_{96}H_{98}O_{33}$: 1778.60 [M]. Found: 1801.4 $[M + Na]^+$.

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