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A simple access to lactose-derived building blocks required in glycoconjugate synthesis

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Abstract

Lactose was readily transformed into thexyldimethylsilyl (3,4-*O*-isopropylidene-β-D-galactopyranosyl)-(1 → 4)-β-D-glucopyranoside (**5**); this compound served as intermediate for the generation of partially *O*-protected lactose building blocks required in oligosaccharide and glycoconjugate synthesis. Thus, from **5** via per-*O*-benzoylation, desilylation, trichloroacetimidate formation, glycosylation of the Lemieux spacer, and acid-catalyzed de-*O*-isopropylidenation methoxycarbonyloctyl (2,6-di-*O*-benzoyl-β-D-galactopyranosyl)-(1 → 4)-2,3,6-tri-*O*-benzoyl-β-D-glucopyranoside (**12**) was obtained. Regioselective benzoylation of **5** with benzoyl cyanide under various conditions afforded 3-*O*- (**13**), 2,3,2′-*O*- (**14**), 3,2′-*O*- (**16**), and 2,2′-*O*-unprotected (**17**) lactoside, respectively. De-*O*-isopropylidenation of **16** gave thexyldimethylsilyl (6-*O*-benzoyl-β-D-galactopyranosyl)-(1 → 4)-2,6-di-*O*-benzoyl-β-D-glucopyranoside (**18**), an important 2′,3′,4′-*O*-unprotected lactose derivative. Fucosylation of **13** and then de-*O*-isopropylidenation afforded thexyldimethylsilyl (2,6-di-*O*-benzoyl-β-D-galactopyranosyl)-(1 → 4)-[(3,4-di-*O*-acetyl-2-*O*-*benzoyl*-α-L-fucopyranosyl)-(1 → 3)]-2,6-di-*O*-benzoyl-β-D-glucopyranoside (**21**), an important fucosyllactose building block. © 1997 Elsevier Science Ltd.

Keywords: Protection, selective; Lactose; Benzoylation; Disaccharide building blocks; Fucosyllactose

1. Introduction

Lactose is an important constituent of the oligosaccharide moiety of various glycoconjugates, especially of glycosphingolipids [1]. Most important is selective access to the 1a-OH group, to the 3b-OH group (*lacto-* and *lactoneo*-series of glycosphingolipids), to the 4b-OH group (*globo*-series), and to the 3b- and 4b-OH groups (*ganglio*-series) (for previous work see ref. [2]). Also, 3a-*O*-fucosylated lactose constituents are quite frequently encountered in oligosaccharides, for instance in human milk oligosaccharides [3]. We have investigated the synthesis of partially *O*-protected lactose and 3a-*O*-fucosyllactose building blocks based on regioselective benzoylation of readily accessible 1-*O*-silyl protected 3b,4b-*O*-isopropylidene lactoside (**5**, Scheme 1) mainly with the help of benzoyl cyanide [4] as mild acylating agent [5,6]. Thus, regioselective oligosaccharide chain extension, simple access to the reducing end of oligosaccharides in order to generate glycosyl donors, and finally convenient removal of the protective groups by simple *O*-deacylation should be possible. Previous

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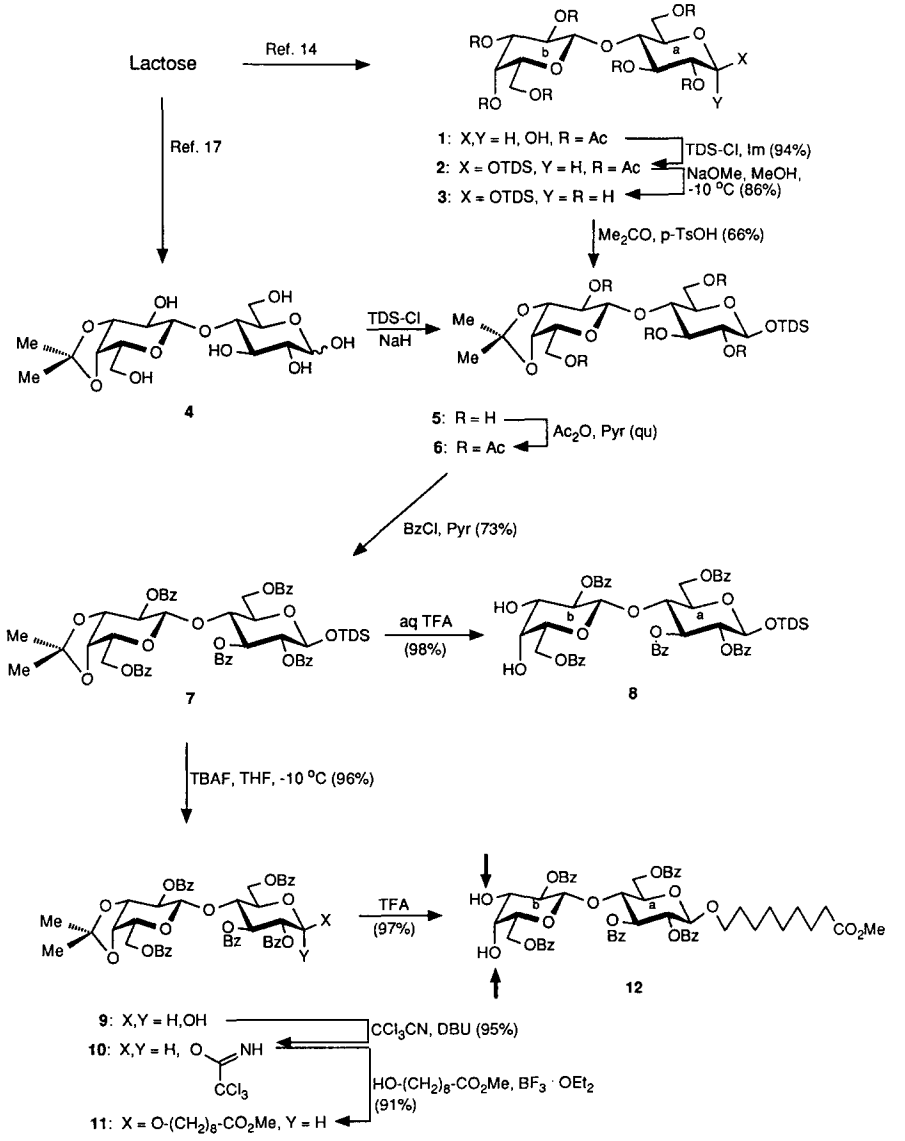
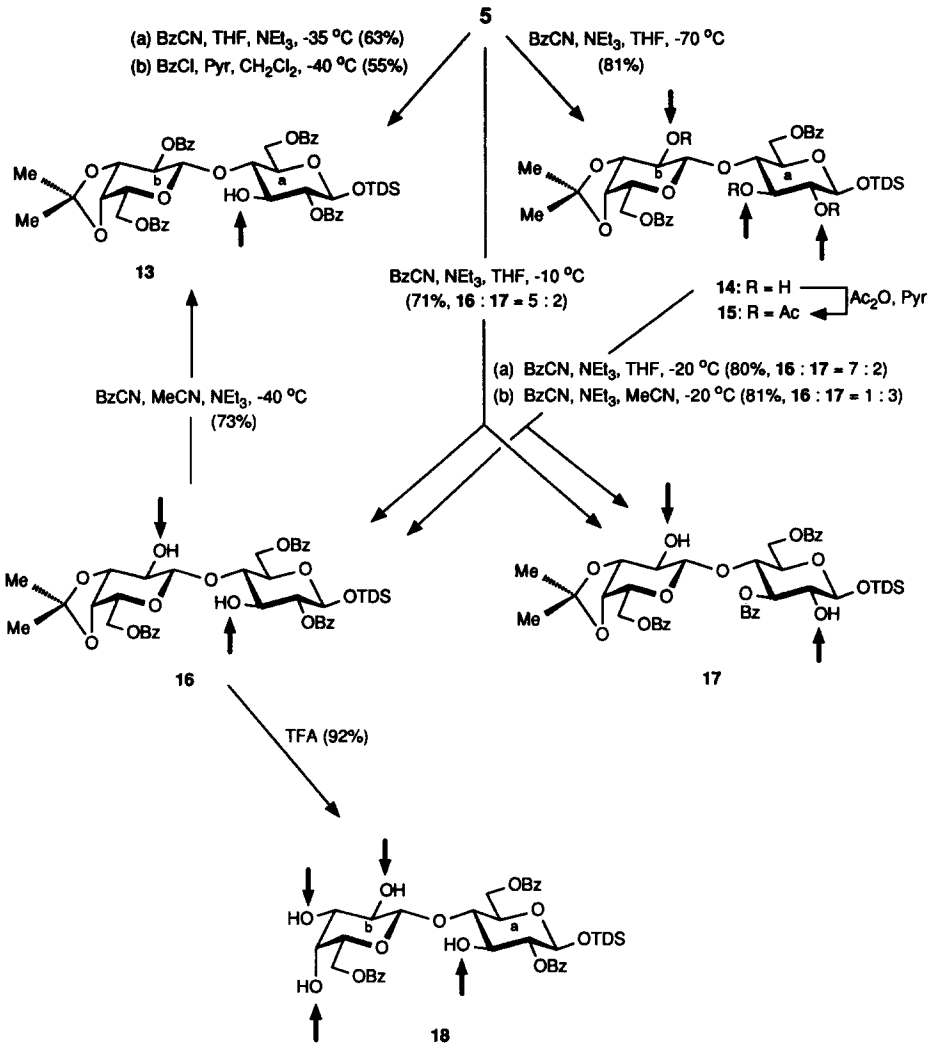
investigations with various alkyl 3b,4b-*O*-isopropylidene lactosides and benzoyl chloride in pyridine as acylating agent exhibited, that the 3a-OH group was least reactive [7,8]. Also other lactose derivatives have been used as substrates in partial *O*-benzoylation reactions [9–13], which also confirmed the low reactivity of the 3a-OH group [9,10].

2. Results and discussion

The important intermediate in our investigations is thexyldimethylsilyl (TDS) 3b,4b-*O*-isopropylidene-lactoside **5** which can be readily obtained from lactose (Scheme 1). Peracetylation of lactose and then regioselective removal of the 1-*O*-acetyl group with hydrazinium acetate following known procedures [14] gave **1**. 1-*O*-Silylation with TDS-Cl in the presence of imidazole afforded silyl β-lactoside **2**. Removal of all *O*-acetyl groups under Zemplén conditions [15] (sodium methoxide/methanol) had to be performed at −10 °C in order to avoid silyl group migration [16], thus furnishing *O*-unprotected silyl β-lactoside **3** in high overall yield. Regioselective 3b,4b-*O*-isopropylidenation could be accomplished with acetone in the presence of *p*-toluenesulfonic acid (*p*-TsOH) as catalyst under reflux conditions; product **5** was structurally confirmed by per-*O*-acetylation with acetic anhydride in pyridine furnishing compound **6** which showed for all *O*-acylated positions the expected ^{1}H NMR low-field shift (H-2a, H-3a, H-6a, H-2b, H-6b; not for H-3b and H-4b). Compound **5**



Scheme 1.



Scheme 2.

could be also obtained in a shorter yet thus far less efficient route. To this aim, lactose was transformed following a known procedure into 3b,4b-*O*-isopropylidene derivative **4** [17]; treatment of **4** with TDS-Cl in the presence of sodium hydride (NaH) furnished **5**.

3b,4b-*O*-Unprotected lactose building blocks could be readily obtained from **5**. Per-*O*-benzoylation of **5** with benzoyl chloride in pyridine afforded intermediate **7**; treatment with aqueous trifluoroacetic acid led to clean de-*O*-isopropylidenation affording 3b,4b-*O*-unprotected **8** in quantitative yield. Desilylation of **7** with tetrabutylammonium fluoride (TBAF) in tetrahydrofuran at −10 °C led to 1a-*O*-unprotected intermediate **9** which gave with trichloroacetonitrile in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as base trichloroacetimidate **10** (2:1, α/β mixture) as lactosyl donor. Ligation with the Lemieux spacer [18] (methyl 9-hydroxy-nonanoate) in the presence of boron trifluoride-ether as catalyst afforded β-lactoside **11** (^{1}H NMR: $J_{1a,2a}$ 7.8 Hz) which on treatment with aqueous trifluoroacetic acid afforded 3b,4b-*O*-unprotected derivative **12**. This compound was extensively employed in the synthesis of *lactoneo*-series oligosaccharides (Lewis X and Lewis Y analogs) [5,6,19].

For the regioselective benzoylation of **5**, benzoyl cyanide as benzoylating agent in the presence of triethylamine as base proved to be particularly successful. Thus, in tetrahydrofuran at −35 °C with excess benzoyl cyanide **5** was directly transformed into 3a-*O*-unprotected derivative **13** (Scheme 2), as could be readily derived from the ^{1}H NMR data (H-3a: δ 3.99) [1]. When the reaction was performed with benzoyl chloride in pyridine at −40 °C also **13**

[1] Similar shifts were observed for structurally related compounds; see ref. [7].

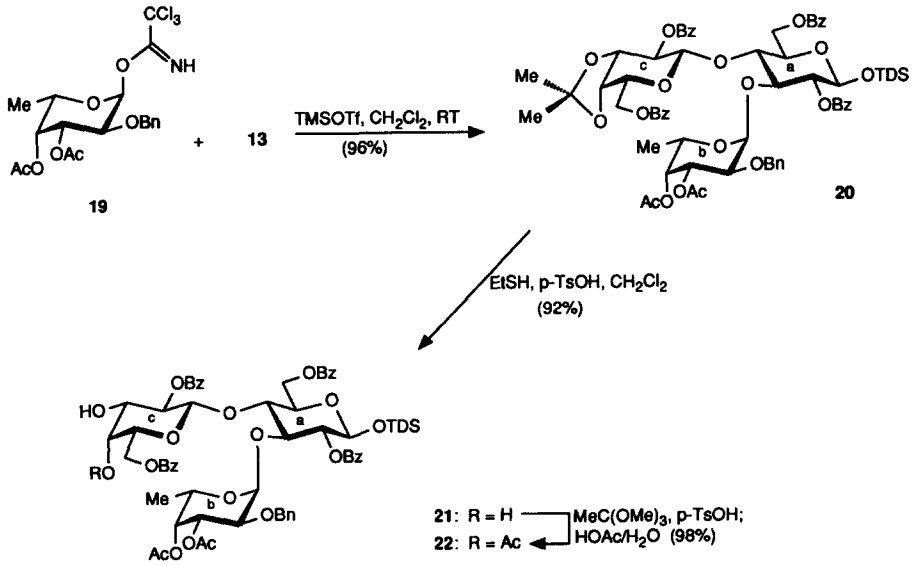
could be obtained, but in lower yield. Reaction of **5** with benzoyl cyanide in tetrahydrofuran in the presence of triethylamine as base at −70 °C afforded 6a,6b-di-*O*-benzoyl derivative **14** in high yield; treatment with acetic anhydride in pyridine furnished **15**. When the reaction of **5** with benzoyl cyanide was carried out at −10 °C two tri-*O*-benzoyl derivatives were obtained in 71% yield, namely the 2a,6a,6b- and the 3a,6a,6b-tri-*O*-benzoyl derivatives **16** and **17** (ratio 5:2). They could be separated by silica gel flash chromatography and structurally assigned (**16**: H-3a, δ 3.88; H-2b, δ 3.64–3.74. **17**: H-2a, δ 3.57; H-2b, δ 3.45). Practically the same result was obtained when **14** was treated with benzoyl cyanide in tetrahydrofuran at −20 °C, furnishing a 7:2 ratio of **16** and **17**. However, when this reaction was carried out in acetonitrile as solvent, the ratio of **16**:**17** (1:3) was dramatically changed in favour of **17**. Thus, exhibiting a variation of the reactivity order in favour of 3a-OH vs. 2a-OH. Benzoylation of **16** in acetonitrile at −40 °C afforded also compound **13** which could be directly obtained from **5**. De-*O*-isopropylidenation of **16** with aqueous trifluoroacetic acid as catalyst furnished 3a,2b,3b,4b-*O*-unprotected derivative **18** which is an interesting intermediate for short and highly efficient GM3-ganglioside syntheses [20,21].

A 3a-*O*-fucosyllactose building block should be readily accessible from intermediate **13** as previously shown for another 3a-*O*-unprotected lactose derivative [8]. In order to obtain a hydrolytically quite stable derivative, fucosylation of **13** was performed with known fucosyl donor **19** [5,19,22] (Scheme 3) under inverse conditions [23,24] with trimethylsilyl trifluoromethanesulfonate (TMSOTf) as catalyst. Thus, the desired α-linked 3a-*O*-fucosyllactoside **20** was obtained in practically quantitative yield. Removal of the 3c,4c-*O*-isopropylidene group was best performed with ethylmercaptan as good nucleophile in the presence of *p*-TsOH as catalyst [25], yielding under mild conditions the 3c,4c-*O*-unprotected intermediate **21**, which offers regioselective access to the 3c-OH and then to the 4c-OH group. In order to ascertain selective reaction at the 3c-OH group, treatment of **21** with methyl ortho-acetate in the presence of *p*-TsOH as acid catalyst and then opening of the cyclic ortho-ester intermediate with aqueous acetic acid following a known procedure [26] was performed. Thus, the 3c-*O*-unprotected compound **22** could be obtained in practically quantitative yield. The structural assignment could be based on the ^{1}H NMR data [H-1a: δ 4.69 (d, $J_{1a,2a}$ 7.8 Hz); H-1b: δ 5.36 (d, $J_{1b,2b}$ 3.8 Hz); H-1c: δ 4.67 (d, $J_{1c,2c}$ 8.1 Hz); H-4b, H-4c: δ 5.42–5.40 (m); H-3c: δ 3.94 (m)].

In conclusion, regioselective benzoylation of silyl 3b,4b-*O*-isopropylidene-lactoside **5** at various temperatures and in different solvents offers in combination with de-*O*-isopropylidenation and/or desilylation interesting building blocks for oligosaccharide and glycoconjugate synthesis.

3. Experimental

Solvents were purified in the usual way. Melting points are uncorrected. TLC was performed on plastic foil plates Silica Gel 60 F_{254} (E. Merck, layer thick-



Scheme 3.

ness 0.2 mm). The detection was achieved by treatment with a soln of 20 g ammonium molybdate and 0.4 g cerium(IV) sulfate in 400 mL 10% H_2SO_4 or with 15% H_2SO_4, and heating at 120 °C. Flash chromatography was carried out on silica gel (Baker, 30–60 μm). Optical rotations were determined at 20 °C with a Perkin–Elmer 241/MC polarimeter (1 dm cell). NMR spectra were recorded with Bruker AC 250 and Bruker 600 DRX instruments, using tetramethylsilane as internal standard.

(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-(1 → 4)-2,3,6-tri-O-acetyl-α/β-D-glucopyranose (**1**). —Compound **1** was synthesized following the procedure previously described [14].

Thexyldimethylsilyl (2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-(1 → 4)-2,3,6-tri-O-acetyl-α/β-D-glucopyranoside (**2**).—To a stirred soln of **1** (93 g, 146 mmol) and imidazole (50 g) in dry Me_2NCHO (300 mL) was added thexyldimethylsilyl chloride (34 mL, 175 mmol). After 24 h the mixture was concd to a 70-mL vol, dild by Et_2O (1.5 L), and washed with a satd aq soln of NH_4Cl (3 × 600 mL). The organic layer was concd in vacuo and the crude product was crystallized from a Et_2O–petroleum ether solvent mixture. Compound **2** (107 g, 94%) was obtained as colourless crystals. TLC (1:1 EtOAc–petroleum ether): R_f 0.62; $[\alpha]_D^{20}$ −8.0° (*c* 1, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): δ 5.32 (dd, 1 H, $J_{3,4}$ 3.4, $J_{4,5} < 1$ Hz, H-4b), 5.18–5.05 (m, 2 H, H-3a,2b), 4.93 (dd, 1 H, $J_{2,3}$ 9.5, $J_{3,4}$ 3.4 Hz, H-3b), 4.83 (dd, 1 H, $J_{1,2}$ 7.6, $J_{2,3}$ 9.6 Hz, H-2a), 4.69 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1a), 4.46–4.41 (m, 2 H, H-6a,1b), 4.14–4.01 (m, 3 H, H-6a, 2 H-6b), 3.84 (m, 1 H, H-5b), 3.72 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.8$ Hz, H-4a), 3.58 (m, 1 H, H-5a), 2.12, 2.07, 2.04, 2.02, 2.01, 1.98, and 1.94 (7 s, 21 H, 7 CH_3CO), 1.55 [mc, 1 H, $HC(CH_3)_2$], 0.80 (m, 12 H, 4 CH_3), 0.10 [2 s, 6 H, $Si(CH_3)_2$]. Anal. Calcd for $C_{34}H_{54}O_{18}Si$ (778.87): C, 52.43; H, 6.99. Found: C, 52.44; H, 6.97.

Thexyldimethylsilyl β-D-galactopyranosyl-(1 → 4)-β-D-glucopyranoside (**3**).—To a soln of **2** (33 g, 43 mmol) in dry MeOH (650 mL) was added a 1 M soln of NaOMe (25 mL). The mixture was stirred at −10 °C for 2 days before being neutralized with Amberlite IR-120, filtered and concd in vacuo. Crystallization in a MeOH–Et_2O mixture (2:1) led to **3** (18 g, 86%) as colourless crystals. TLC (65:30:5 $CHCl_3$–MeOH–H_2O): R_f 0.42; $[\alpha]_D^{20}$ +3.0° (*c* 1, MeOH); ^1H NMR (250 MHz, D_2O): δ 4.53 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1a), 4.29 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1b), 3.9–3.3 (m, 11 H, H-3a,4a,5a, 2 H-6a, H-2b,3b,4b,5b, 2 H-6b), 3.07 (dd, 1 H, $J_{1,2}$ 7.6, $J_{2,3}$ 8.4 Hz, H-2a), 1.50 [mc, 1 H, $HC(CH_3)_2$], 0.71 (m, 12 H, 4 CH_3), 0.06 [1 s, 6 H, $Si(CH_3)_2$]. Anal. Calcd for $C_{20}H_{40}O_{11}Si \cdot 0.5H_2O$ (493.61): C, 48.66; H, 8.37. Found: C, 48.58; H, 8.45.

Thexyldimethylsilyl (3,4-O-isopropylidene-β-D-galactopyranosyl)-(1 → 4)-β-D-glucopyranoside (**5**). —*(a) From* **3**. A soln of **3** (2.8 g, 5.75 mmol) and anhyd *p*-TsOH (0.2 mL) in dry acetone (150 mL) was stirred for 15 min under reflux. Then the mixture was cooled to room temperature before being neutralized with solid $NaHCO_3$ (1 g). After filtration and concn in vacuo, a flash chromatography column (9:1 EtOAc–MeOH) of the residue led to **5** (2.0 g, 66%) as a colourless foam. TLC (5:1 EtOAc–MeOH): R_f 0.7.

(b) From **4**. To a cooled (−15 °C) soln of **4** [17] (1.0 g, 2.6 mmol) in dry Me_2NCHO, NaH (68 mg, 2.86 mmol) was added, and the mixture was stirred for 10 min. Then the soln of thexyldimethylsilyl chloride (560 μL, 2.86 mmol) in dry Me_2NCHO (3 mL) was added dropwise. After 1 h (at −15 °C) the mixture was neutralized with $NaHCO_3$ and concd in vacuo. The resulting residue was purified by flash chromatography (9:1 EtOAc–MeOH) to yield **5** (350 mg, 25%) as an α/β mixture (1:4); $[\alpha]_D^{20}$ +22.0° (*c* 1, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$), β anomer: δ 4.55 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1a), 4.39 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1b), 4.2–3.2 (m, 12 H, H-2a,3a,4a,5a, 2 H-6a, H-2b,3b,4b,5b, 2 H-6b), 1.64 [mc, 1 H, $HC(CH_3)_2$], 1.52 (s, 3 H, CH_3), 1.32 (s, 3 H, CH_3), 0.88 (m, 12 H, 4 CH_3), 0.19 [s, 6 H, $Si(CH_3)_2$]. Anal. Calcd for $C_{23}H_{44}O_{11}Si$ (524.67): C, 52.65; H, 8.45. Found: C, 52.58; H, 8.37.

Thexyldimethylsilyl (2,6-di-O-acetyl-3,4-O-isopropylidene-β-D-galactopyranosyl)-(1 → 4)-2,3,6-tri-O-acetyl-β-D-glucopyranoside (**6**).—Compound **5** (200 mg, 381 μmol) was dild in a pyridine–Ac_2O mixture (1:1, 30 mL) and stirred overnight at room temperature. The mixture was concd in vacuo and coevaporated with toluene. Flash chromatography (9:1 toluene–acetone) yielded **6** (250 mg, 89%). TLC (8:2 toluene–acetone): R_f 0.60; $[\alpha]_D^{20}$ +15.7° (*c* 1, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): δ 5.13 (dd, 1 H, $J_{2,3}$ 9.4, $J_{3,4}$ 8.7 Hz, H-3a), 4.84 (m, 2 H, H-2a,2b), 4.67 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1a), 4.50–4.00 (m, 7 H, 2 H-6a, H-1b,3b,4b, 2 H-6b), 3.91 (m, 1 H, H-5b), 3.67 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.9$ Hz, H-4a), 3.59 (m, 1 H, H-5a), 2.15–1.98 (5 s, 5 CH_3CO), 1.57 [mc, 1 H, $HC(CH_3)_2$], 1.51 (s, 3 H, CH_3), 1.29 (s, 3 H, CH_3), 0.80 (m, 12 H, 4 CH_3), 0.09 [2 s, 6 H, $Si(CH_3)_2$]. Anal. Calcd for $C_{33}H_{54}O_{16}Si$ (734.85): C, 53.93; H, 7.41. Found: C, 53.91; H, 7.35.

Thexyldimethylsilyl (2,6-di-O-benzoyl-3,4-O-isopropylidene-β-D-galactopyranosyl)-(1 → 4)-2,3,6-tri-O-benzoyl-β-D-glucopyranoside (**7**).—Benzoyl chloride (250 μL, 2.09 mmol) was added to a soln of **5** (200 mg, 380 μmol) in dry pyridine at 0 °C. The mixture was stirred for 3 days at room temperature, dild with EtOAc (20 mL), and washed with a satd aq soln of NH_4HCO_3 (20 mL). The aq layer was extracted with EtOAc (20 mL). The combined organic layers were concd in vacuo and the residue was purified by flash chromatography (95:5 toluene–acetone). Compound **7** (370 mg, 73%) was obtained from Et_2O as colourless crystals. TLC (95:5 toluene–acetone): R_f 0.45; $[\alpha]_D^{20}$ +43.0° (*c* 1, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): δ 8.2–7.2 (m, 25 H, 5 C_6H_5CO), 5.67 (dd, 1 H, $J_{2,3} = J_{3,4} = 9.8$ Hz, H-3a), 5.36 (dd, 1 H, $J_{1,2}$ 7.6, $J_{2,3}$ 9.8 Hz, H-2a), 5.12 (dd, 1 H, $J_{1,2} = J_{2,3} = 7.7$ Hz, H-2b), 4.89 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1a), 4.7–4.5 (m, 2 H, $J_{1,2}$ 7.7 Hz, H-6a,1b), 4.48–4.38 (m, 1 H, H-6a), 4.3–4.0 (m, 4 H, H-4a,3b,4b,6b), 3.81 (m, 2 H, H-5a,5b), 3.66–3.58 (dd, 1 H, H-6b), 1.50 (s, 3 H, CH_3), 1.42 [mc, 1 H, $HC(CH_3)_2$], 1.23 (s, 3 H, CH_3), 0.65 (m, 12 H, 4 CH_3), 0.0 [2 s, 6 H, $Si(CH_3)_2$]. Anal. Calcd for $C_{58}H_{64}O_{16}Si$ (1045.22): C, 66.65; H, 6.17. Found: C, 66.52; H, 6.15.

Thexyldimethylsilyl (2,6-di-O-benzoyl-β-D-galactopyranosyl)-(1 → 4)-2,3,6-tri-O-benzoyl-β-D-glucopyranoside (**8**).—An aq 50% soln of CF_3CO_2H (10 mL) was added to a stirred soln of **7** (2 g, 1.91 mmol) in CH_2Cl_2 (70 mL). After 5 h at room temperature the mixture was neutralized with a satd aq soln of $NaHCO_3$ (100 mL). The aq layer was extracted with CH_2Cl_2 (100 mL) and the combined organic layers were concd in vacuo. The residue was purified by flash chromatography (85:15 toluene–acetone). Compound **8** (1.89 g, 98%) was obtained as a colourless foam. TLC (9:1 toluene–acetone): R_f 0.10; $[\alpha]_D^{20}$ +40.5° (*c* 1, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): δ 8.2–7.2 (m, 25 H, 5 C_6H_5CO), 5.6 (dd, 1 H, $J_{2,3} = J_{3,4} = 9.7$ Hz, H-3a), 5.4–5.3 (m, 2 H, H-2a,2b), 4.87 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1a), 4.55 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1b), 4.48–4.46 (m, 2 H, 2 H-6a), 4.10–3.90 (m, 2 H, H-4a,6b), 3.80–3.70 (m, 2 H, H-5a,4b), 3.68 (dd, 1 H, $J_{2,3}$ 9.9, $J_{3,4}$ 3.6 Hz, H-3b), 3.6–3.4 (m, 2 H, H-5b,6b), 1.41 [mc, 1 H, $HC(CH_3)_2$], 0.64 (m, 12 H, 4 CH_3), 0.02–0.01 [2 s, 6 H, $Si(CH_3)_2$]. Anal. Calcd for $C_{55}H_{60}O_{16}Si$ (1005.15): C, 65.72; H, 6.02. Found: C, 65.75; H, 6.09.

(2,6-Di-O-benzoyl-3,4-O-isopropylidene-β-D-galactopyranosyl)-(1 → 4)-2,3,6-tri-O-benzoyl-α / β-D-glucopyranose (**9**).—A 1 M soln of tetrabutylammonium fluoride (1.1 mL) was added dropwise to a soln of **7** (1 g, 0.96 mmol) in dry THF (20 mL) at −10 °C. The mixture was stirred for 2 h before being dild with EtOAc (50 mL) and washed with a satd aq soln of NH_4HCO_3 (50 mL). The aq layer was extracted with EtOAc (50 mL). The organic layers were combined and concd in vacuo. The residue, purified by flash chromatography (9:1 toluene–acetone), led to **9** (830 mg, 96%) as a colourless foam. TLC (9:1 toluene–acetone): R_f 0.27; $[\alpha]_D^{20}$ +72.0° (*c* 1, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): δ 8.2–7.2 (m, 25 H, 5 C_6H_5CO), 6.05 (dd, 1 H, $J_{2,3} = J_{3,4} = 9.6$ Hz, H-3a), 5.7–3.7 (m, 13 H, H-1a,2a,4a,5a, 2 H-6a, H-1b,2b,3b,4b,5b, 2 H-6b), 2.92 (bs, 1 H, OH), 1.49–1.23 (2 s, 6 H, 2 CH_3). Anal. Calcd for $C_{50}H_{45}O_{16}$ (901.89): C, 66.58; H, 5.03. Found: C, 66.51; H, 5.06.

(2,6-Di-O-benzoyl-3,4-O-isopropylidene-β-D-galactopyranosyl)-(1 → 4)-2,3,6-tri-O-benzoyl-α / β-D-glucopyranosyl trichloroacetimidate (**10**).—To a soln of **9** (10 g, 11 mmol) in dry CH_2Cl_2 (250 mL) were added trichloroacetonitrile (20 mL) and DBU (2 drops). The reaction mixture was stirred for 3 h and concd in vacuo. Flash chromatography (8:92 toluene–acetone) of the residue led to **10** (11 g, $\alpha/\beta \approx 2:1$, 95%) as a colourless foam. TLC (9:1 toluene–acetone): R_f 0.52; $[\alpha]_D^{20}$ +69° (*c* 1, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): δ 8.59 (s, 1/3 H, NH), 8.53 (s, 2/3 H, NH), 8.2–7.2 (m, 25 H, 5 C_6H_5CO), 6.68 (d, 1 H, $J_{1,2}$ 3.7 Hz, H α-1a), 6.2–3.6 [m, 13 H, H-2a,3a,4a,5a, 2 H-6a, 4.70 (d, 1 H, $J_{1,2}$ 7.4 Hz, H-1b), H-2b,3b,4b,5b, 2 H-6b], 1.48 (s, 3 H, CH_3), 1.23 (s, 3 H, CH_3). Anal. Calcd for $C_{52}H_{455}Cl_3NO_{16}$ (1046.28): C, 59.69; H, 4.31; N, 1.34. Found: C, 59.50; H 4.44; N 1.42.

8-Methoxycarbonyloctyl (2,6-di-O-benzoyl-3,4-O-isopropylidene-β-d-galactopyranosyl)-(1 → 4)-2,3,6-tri-O-benzoyl-β-D-glucopyranoside (**11**).—Trichloroacetimidate **10** (10 g, 9.6 mmol) and methyl 9-hydroxynonanoate [18] (4 mL, ≈ 21 mmol) were dild in dry CH_2Cl_2 (25 mL), and a 0.5 M soln of boron trifluoride in Et_2O (0.5 mL) was added. The mixture was allowed to react for 2 h, dild with CH_2Cl_2 (100 mL), and washed with a satd aq soln of $NaHCO_3$. The aq layer was extracted twice with CH_2Cl_2 (50 mL). The combined organic layers were concd in vacuo. Flash chromatography (96:4 → 92:8 toluene–acetone) of the residue led to pure **11** (9.1 g, 91%). TLC (75:25 petroleum ether–EtOAc): R_f 0.16; $[\alpha]_D^{20}$ +43.0° (*c* 1, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): δ 8.2–7.2 (m, 25 H, 5 C_6H_5CO), 5.69 (dd, 1 H,

$J_{2,3} = J_{3,4} = 9.5$ Hz, H-3a), 5.39 (dd, 1 H, $J_{2,3}$ 9.6 Hz, H-2a), 5.11 (dd, 1 H, $J_{1,2} = J_{2,3} = 7.4$ Hz, H-2b), 4.61–4.54 [m, 3 H, H-1a ($J_{1,2}$ 7.8 Hz), H-6a,1b ($J_{1,2}$ 7.4 Hz)], 4.48–4.38 (dd, 1 H, H-6a), 4.25–4.13 (m, 3 H, H-4a,3b,6b), 4.04 (dd, 1 H, $J_{3,4}$ 5.6, $J_{4,5}$ 1.9 Hz, H-4b), 3.9–3.3 (m, 8 H, O–CH_2–CH_2, $COOCH_3$, H-5a,5b,6b), 2.19 (dd, 2 H, $J = J = 7.5$ Hz, CH_2–CH_2–COO), 1.49–1.22 (m, 10 H, 2 CH_3, O–CH_2–CH_2, CH_2–CH_2–COO), 1.03 (m, 8 H, 4 CH_2). Anal. Calcd for $C_{59}H_{63}O_{18}$ (1060.13): C, 66.84; H, 5.99. Found: C, 66.92; H, 6.05.

8-Methoxycarbonyloctyl (2,6-di-O-benzoyl-β-D-galactopyranosyl)-(1 → 4)-2,3,6-tri-O-benzoyl-β-D-glucopyranoside (**12**).—An aq 50% soln of CF_3CO_2H (2 mL) was added to a soln of **11** (150 mg, 0.141 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred for 6 h and neutralized with a satd aq soln of $NaHCO_3$ (30 mL). The aq layer was extracted with CH_2Cl_2 (50 mL). The combined organic layers were concd in vacuo. Flash chromatography (95:5 → 9:1 toluene–acetone) of the residue led to pure **12** (140 mg, 97%) as a colourless foam. TLC (4:6 petroleum ether–EtOAc): R_f 0.49; $[\alpha]_D^{20}$ +35.0° (*c* 1, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.2–7.2 (m, 25 H, 5 C_6H_5CO), 5.64 (dd, 1 H, $J_{3,4}$ 9.7 Hz, H-3a), 5.39 (dd, 1 H, $J_{1,2}$ 8.0, $J_{2,3}$ 9.7 Hz, H-2a), 5.26 (dd, 1 H, $J_{1,2}$ 8.0, $J_{2,3}$ 9.8 Hz, H-2b), 4.7–4.4 [m, 4 H, H-1a ($J_{1,2}$ 8.0 Hz), H-1b ($J_{1,2}$ 8.0 Hz), 2 H-6a], 4.09 (dd, 1 H, $J_{3,4} = J_{4,5} = 9.7$ Hz, H-4a), 3.98 (dd, 1 H, J_{gem} 10.3, $J_{5,6}$ 5.3 Hz, H-6b), 3.81–3.3 (m, 10 H, O–CH_2–CH_2, $COOCH_3$, H-5a,3b,4b,5b,6b), 2.19 (dd, 2 H, *J* 7.5 Hz, CH_2–CH_2–COO), 1.51–1.39 (m, 4 H, OCH_2–CH_2, CH_2–CH_2–COO), 1.03 (m, 8 H, 4 CH_2). Anal. Calcd for $C_{56}H_{59}O_{18}$ (1020.07): C, 65.94; H, 5.83. Found: C, 65.83; H, 5.92.

Thexyldimethylsilyl (2,6-di-O-benzoyl-3,4-O-isopropylidene-β-D-galactopyranosyl)-(1 → 4)-2,6-di-O-benzoyl-β-D-glucopyranoside (**13**).—*(a) From* **5** *with benzoyl cyanide.* To a soln of **5** (1.3 g, 2.47 mmol) in dry THF (20 mL) cooled at −35 °C, Et_3N (6 mL) was added. A freshly prepared soln of benzoyl cyanide (3.56 g, 27.17 mmol) in dry THF (30 mL) was added portionwise and dropwise, monitoring carefully the reaction progress on TLC. After 36 h the mixture was allowed to warm at room temperature, dild with EtOAc (300 mL), and washed with a satd aq NH_4HCO_3 soln (3 × 200 mL). The combined aq layers were reextracted with EtOAc (2 × 100 mL), then the organic layers were dried ($MgSO_4$) and concd in vacuo. Flash chromatography (9:1 toluene–EtOAc) gave **13** (1.46 g, 63%) as a foam. TLC (8:2 toluene–acetone): R_f 0.77; $[\alpha]_D^{20}$ +31.3° (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.15–7.25 (m, 20 H, 4 C_6H_5CO), 5.36 (dd, 1 H, $J_{1b,2b}$ 8.2, $J_{2b,3b}$ 7.8 Hz, H-2b), 5.16 (dd, 1 H, $J_{1a,2a}$ 7.7, $J_{2a,3a}$ 9.5 Hz, H-2a), 4.87 (dd, 1 H, J_{gem} 12.3, $J_{6b,5b}$ 2.1 Hz, H-6b), 4.78 (d, 1 H, $J_{1a,2a}$ 7.7 Hz, H-1a), 4.64 (d, 1 H, $J_{1b,2b}$ 8.2 Hz, H-1b), 4.55 (bs, 1 H, OH exch. with D_2O), 4.45–4.38 (m, 2 H, H-3b,6b), 4.32–4.19 (m, 4 H, H-5b,4b, 2 H-6a), 3.95 (dd, 1 H, $J_{2a,3a}$ 9.5, $J_{3a,4a}$ 7.8 Hz, H-3a), 3.71–3.59 (m, 2 H, H-4a,5a), 1.65 [s, 3 H, $C(CH_3)_2$ isoprop.], 1.42 [m, 1 H, $HC(CH_3)_2$ thexyl], 1.36 [s, 3 H, $C(CH_3)_2$ isoprop.], 0.70–0.62 [m, 12 H, $C(CH_3)_2$ thexyl, $SiC(CH_3)_2$], 0.02 and −0.03 [2 s, 6 H, $Si(CH_3)_2$]. Anal. Calcd for $C_{51}H_{60}O_{15}Si$: C, 65.08; H, 6.42. Found: C, 65.22; H, 6.60.

(b) From **5** *with benzoyl chloride.* To a soln of **5** (1.0 g, 1.9 mmol) in dry CH_2Cl_2 (5 mL), cooled at −40 °C, pyridine (3 mL) was added. A freshly prepared soln of benzoyl chloride (1.07 g, 7.6 mmol) in dry CH_2Cl_2 (10 mL) was added dropwise. After 7 h, MeOH (10 mL) was added and the mixture was allowed to warm to room temperature, dild with CH_2Cl_2 (50 mL), and washed with H_2O (2 × 100 mL). The aq phases were reextracted with CH_2Cl_2 (2 × 40 mL) and finally the organic phases washed once more with brine (100 mL). After drying ($MgSO_4$) and evaporation of the solvent, flash chromatography (9:1 toluene–EtOAc) gave **13** (995 mg, 55%) as a foam. For physical data, see (*a*).

(c) From **16**. To a soln of **16** (200 mg, 0.24 mmol) in dry CH_3CN (2.5 mL) cooled at −40 °C, was added Et_3N (1 mL). A freshly prepared soln of benzoyl cyanide (125 mg, 0.956 mmol) in dry CH_3CN (8 mL) was added dropwise, monitoring carefully the reaction progress on TLC. After 36 h the mixture was dild with EtOAc (60 mL), allowed to warm to room temperature, and washed with a satd aq NH_4HCO_3 soln (3 × 60 mL). The aq phases were reextracted with EtOAc (30 mL) and the combined organic phases were dried ($MgSO_4$) and concd in vacuo. Flash chromatography (9:1 toluene–EtOAc) afforded **13** (163 mg, 73%) as a foam. For physical data, see (*a*).

Thexyldimethylsilyl (6-O-benzoyl-3,4-O-isopropylidene-β-D-galactopyranosyl)-(1 → 4)-6-O-benzoyl-β-D-glucopyranoside (**14**).—To a soln of **5** (1 g, 381 μmol) in dry THF was added at −70 °C Et_3N (15 mL). Then a soln of benzoyl cyanide (160 mg, 1.26 mmol) in dry THF was added dropwise. After 10 h the mixture was dild with EtOAc (50 mL) and washed with a satd aq soln of $NaHCO_3$ (2 × 70 mL). The aq layer was extracted with EtOAc (50 mL). The combined organic layers were concd in vacuo and the residue was purified by flash chromatography (8:2

toluene–acetone). Compound **14** (1.1 g, 81%) was obtained as a colourless foam. TLC (8:2 toluene–acetone): R_f 0.36; $[\alpha]_D^{20}$ +35.0° (*c* 1, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$, H → D): δ 8.20–7.30 (m, 10 H, 2 C_6H_5CO), 4.95–3.27 (m, 14 H, H-1a,2a,3a,4a,5a, 2 H-6a, H-1b,2b,3b,4b,5b, 2 H-6b), 1.71–1.54 [mc, 1 H, $HC(CH_3)_2$], 1.54 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3), 0.86–0.83 (m, 12 H, 4 CH_3), 0.14–0.12 [2 s, 6 H, $Si(CH_3)_2$]. Anal. Calcd for $C_{37}H_{52}O_{13}Si$ (732.89): C, 60.93; H, 7.15. Found: C, 60.65; H, 7.14.

Thexyldimethylsilyl (2-O-acetyl-6-O-benzoyl-3,4-O-isopropylidene-β-D-galactopyranosyl)-(1 → 4)-2,3-di-O-acetyl-6-O-benzoyl-β-D-glucopyranoside (**15**).—Compound **14** (150 mg, 204 μmol) was stirred overnight in a mixture of pyridine (20 mL) and Ac_2O (10 mL). Concentration in vacuo and coevaporation (twice) with toluene led to a residue which was purified by flash chromatography (95:5 toluene–acetone), yielding **15** (165 mg, 94%) as a colourless foam. TLC (9:1 toluene–acetone): R_f 0.43; $[\alpha]_D^{20}$ +28.0° (*c* 1, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): δ 8.10–7.32 (m, 10 H, C_6H_5CO), 5.21 (dd, 1 H, $J_{2,3} = J_{3,4} = 9.4$ Hz, H-3a), 4.93–4.86 (m, 2 H, H-2a,2b), 4.73–4.64 (m, 3 H, H-1a,6a,6b), 4.43–4.30 (m, 3 H, H-6a,1b,6b), 4.16–4.07 (m, 2 H, H-3b,4b), 3.94 (m, 1 H, H-5b), 3.82–3.70 (m, 2 H, H-4a,5a), 2.06–2.00 (3 s, 9 H, 3 CH_3CO), 1.53 [m, 4 H, CH_3, $HC(CH_3)_2$], 1.29 (s, 3 H, CH_3), 0.80–0.76 (m, 12 H, 4 CH_3), 0.06 [2 s, 6 H, $Si(CH_3)_2$]. Anal. Calcd for $C_{43}H_{58}O_{16}Si$ (859.00): C, 60.13; H, 6.80. Found: C, 60.03; H, 6.79.

Thexyldimethylsilyl (6-O-benzoyl-3,4-O-isopropylidene-β-D-galactopyranosyl)-(1 → 4)-2,6-di-O-benzoyl-β-D-glucopyranoside (**16**) *and Thexyldimethylsilyl (6-O-benzoyl-3,4-O-isopropylidene-β-D-galactopyranosyl)-(1 → 4)-3,6-di-O-benzoyl-β-D-glucopyranoside* (**17**).—*(a) From* **14** in THF as solvent. To a soln of **14** (200 mg, 273 μmol) in dry THF (8 mL), cooled at −20 °C, was added Et_3N (4 mL). Then a soln of benzoyl cyanide (100 mg) in dry CH_3CN was added dropwise. The mixture was stirred for 14 h, dild with EtOAc (50 mL), and washed with a satd aq soln of $NaHCO_3$ (2 × 70 mL). The aq layer was extracted with EtOAc (50 mL) and the combined organic layers were concd in vacuo. The residue was separated by flash chromatography (95:5 → 9:1 toluene–acetone), and **16** and **17** were obtained in a 7:2 ratio (195 mg, 86%) as colourless foams.

16: TLC (8:2 toluene–acetone): R_f 0.49.

17: TLC (8:2 toluene–acetone): R_f 0.39.

(b) From **14** *in CH_3CN as solvent.* To a soln of **14** (100 mg, 136 μmol) in dry CH_3CN (5 mL), cooled at −20 °C, was added Et_3N (2 mL). Then a soln of benzoyl cyanide (30 mg) in dry CH_3CN was added dropwise. The mixture was stirred for 14 h, dild with EtOAc (50 mL), and washed with a satd aq soln of $NaHCO_3$ (2 × 40 mL). The aq layer was extracted with EtOAc (50 mL) and the combined organic layers were concd in vacuo. The residue was separated by flash chromatography (8:2 toluene–acetone), and **16** and **17** were obtained in a 1:3 ratio (93 mg, 81%) as a colourless foam.

(c) From **5**. To a soln of **5** (1.0 g, 1.9 mmol) in dry THF (15 mL), cooled at −25 °C, was added Et_3N (2.5 mL). A freshly prepared soln of benzoyl cyanide (1.24 g, 9.5 mmol) in dry THF (18 mL) was added dropwise, monitoring carefully the reaction progress on TLC. After 16 h the mixture was dild with EtOAc (300 mL), then allowed to warm to room temperature and washed with a satd aq NH_4HCO_3 soln (2 × 200 mL). The combined aq layers were reextracted with EtOAc (2 × 100 mL), then the organic layers were dried ($MgSO_4$) and concd in vacuo. Flash chromatography (9:1 → 8:2 toluene–acetone) gave **16** (943 mg, 59%) and **17** (360 mg, 22%) as foams.

16: TLC (8:2 toluene–acetone): R_f 0.46; $[\alpha]_D^{20}$ +29° (*c* 1, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$, H → D): δ 8.2–7.26 (m, 15 H, C_6H_5CO), 5.17 (dd, 1 H, $J_{1,2}$ 7.7, $J_{2,3}$ 9.8 Hz, H-2a), 4.98–4.90 (m, 1 H, H-6a), 4.81–4.76 [m, 2 H, H-1a ($J_{1,2}$ 7.8 Hz), H-6a], 4.39–4.29 (m, 3 H, H-6a,1b,6b), 4.19–4.10 (m, 3 H, H-3b,4b,5b), 3.88 (dd, 1 H, $J_{2,3}$ 9.8, $J_{3,4}$ 8.2 Hz, H-3a), 3.74–3.64 (m, 2 H, H-5a,2b), 3.52 (dd, 1 H, $J_{3,4}$ 8.2, $J_{4,5}$ 9.5 Hz, H-4a), 1.53 (s, 3 H, CH_3), 1.46 [mc, 1 H, $HC(CH_3)_2$], 1.34 (s, 3 H, CH_3), 0.69–0.66 (m, 12 H, 4 CH_3), 0.10–0.02 [2 s, 6 H, $Si(CH_3)_2$]. Anal. Calcd for $C_{44}H_{56}O_{14}Si$ (837.00): C, 63.14; H, 6.74. Found: C, 62.95; H, 6.75.

17: TLC (8:2 toluene–acetone): R_f 0.39; $[\alpha]_D^{20}$ −8.0° (*c* 1, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$, H → D): δ 8.2–7.26 (m, 15 H, C_6H_5CO), 5.40 (dd, 1 H, $J_{2,3} = J_{3,4} = 9.4$ Hz, H-3a), 4.82 (dd, 1 H, $J_{5,6}$ 1.8, J_{gem} 11.5 Hz, H-6a), 4.78 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1a), 4.46 (dd, 1 H, $J_{5,6}$ 5.9, J_{gem} 11.5 Hz, H-6a), 4.26 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1b), 4.19 (dd, 1 H, $J_{5,6}$ 4.1, J_{gem} 10.2 Hz, H-6b), 4.04–3.95 (m, 3 H, H-3b,4b,6b), 3.89–3.79 (m, 3 H, H-4a,5a,5b), 3.57 (dd, 1 H, $J_{1,2}$ 7.5, $J_{2,3}$ 9.7 Hz, H-2a), 3.45 (dd, 1 H, $J_{1,2}$ 8.0, $J_{2,3}$ 6.4 Hz, H-2b), 1.57 [mc, 1 H, $HC(CH_3)_2$], 1.35 (s, 3 H, CH_3), 1.22 (s, 3 H, CH_3), 0.85–0.81 (m, 12 H, 4 CH_3), 0.12 [2 s, 6 H, $Si(CH_3)_2$].

Thexyldimethylsilyl (6-O-benzoyl-β-D-galactopyranosyl)-(1 → 4)-2,6-di-O-benzoyl-β-D-

glucopyranoside (**18**).—An aq 50% soln of CF_3CO_2H (4 mL) was added to a soln of **16** (330 mg, 394 μmol) in CH_2Cl_2 (20 mL). The mixture was stirred for 7 h at room temperature, dild by CH_2Cl_2 (50 mL), and neutralized with a satd aq soln of $NaHCO_3$ (70 mL). The aq layer was extracted with CH_2Cl_2 (50 mL) and the combined organic layers were concd in vacuo. Flash chromatography (7:3 → 6:4 toluene–acetone) of the residue led to pure **18** (290 mg, 92%) as a colourless foam. TLC (1:1 toluene–acetone): R_f 0.22; $[\alpha]_D^{20}$ +19.0° (*c* 1, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 5.12 (dd, 1 H, $J_{1a,2a} = J_{2a,3a} = 9.1$ Hz, H-2a), 5.03 (s, 1 H, OH-2b), 4.97 (s, 1 H, OH-3b), 4.93–4.84 (m, 2 H, 2 H-6a), 4.77 (d, 1 H, $J_{1a,2a}$ 9.1 Hz, H-1a), 4.67 (s, 1 H, OH-3a), 4.68–4.60 (m, 1 H, H-6b,6'b), 4.40–4.28 (m, 4 H, 2 H-6a, 2 H-6b), 4.34 (d, 1 H, $J_{1b,2b}$ 9.5 Hz, H-1b), 4.33 (s, 1 H, OH-4b), 3.95 (dd, 1 H, $J_{3b,4b} = J_{4b,5b} = 1.1$ Hz, H-4b), 3.91 (dd, 1 H, $J_{1b,2b}$ 9.5, $J_{2b,3b}$ 9.1 Hz, H-2b), 3.90 (dd, 1 H, $J_{2a,3a}$ 9.1, $J_{3a,4a}$ 9.3 Hz, H-3a), 3.83 (m, 1 H, H-5b), 3.82 (m, 1 H, H-5a), 3.67 (dd, 1 H, $J_{2b,3b}$ 9.1, $J_{3b,4b}$ 1.1 Hz, H-3b), 3.51 (dd, 1 H, $J_{3a,4a} = J_{4a,5a} = 9.3$ Hz, H-4a), 1.46 [mc, 1 H, $HC(CH_3)_2$], 0.69–0.62 (m, 12 H, 4 CH_3), 0.04–0.02 [2 s, 6 H, $Si(CH_3)_2$]. Anal. Calcd for $C_{41}H_{52}O_{14}Si$ (796.94): C, 61.79; H, 6.58. Found: C, 61.71; H, 6.57.

Thexyldimethylsilyl (2,6-di-O-benzoyl-3,4-O-isopropylidene-β-D-galactopyranosyl)-(1 → 4)-[(3,4-di-O-acetyl-2-O-benzyl-α-L-fucopyranosyl)-(1 → 3)]-2,6-di-O-benzoyl-β-D-glucopyranoside (**20**).—To a soln of **13** (1 g, 1.062 mmol) in dry CH_2Cl_2 (4 mL) cooled to 0 °C in an ice bath, was added a freshly prepared 0.1 M soln of Me_3SiOTf in dry CH_2Cl_2 (106 μL), and thereafter a soln of **19** [19,22] (1.025 g, 2.12 mmol) in dry CH_2Cl_2 (15 mL) was added dropwise with stirring at room temperature. The mixture was neutralized with Et_3N and concd in vacuo. Flash chromatography (95:5 toluene–acetone) gave **20** (1.28 g, 96%) as a white powdery solid. TLC (9:1 toluene–acetone): R_f 0.47; mp 89–90 °C; $[\alpha]_D^{20}$ −9.8° (*c* 1.4, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 8.18–6.80 (m, 25 H, 5 C_6H_5CO), 5.40–5.26 (m, 4 H, H-1b,3b,4b,2a), 5.25 (dd, 1 H, $J_{1c,2} = J_{2c,3c} = 8.2$ Hz, H-2c), 5.12 (m, 1 H, H-5b), 4.98–4.90 (m, 1 H, H-6c), 4.83–4.76 (m, 1 H, H-6c), 4.67 (d, 1 H, $J_{1a,2a}$ 7.4 Hz, H-1a), 4.58–4.50 (m, 1 H, H-6a), 4.50 (d, 1 H, $J_{1c,2c}$ 8.2 Hz, H-1c), 4.44–4.35 (m, 1 H, H-6a), 4.30 (d, 1 H, J_{gem} 12.2 Hz, 1/2 CH_2Ph), 4.27–4.21 (m, 1 H, H-3c), 4.21–4.18 (m, 2 H, H-3a,4c), 4.01–3.92 (m, 3 H, H-5c,4a, 1/2 CH_2Ph), 3.66–3.59 (m, 1 H, H-2b), 3.55–3.49 (m, 1 H, H-5a), 2.00 and 1.74 (2 s, 6 H, 2 CH_3CO), 1.57 [s, 3 H, $C(CH_3)_2$ isoprop.], 1.38–1.35 [m, 1 H, $HC(CH_3)_2$ thexyl], 1.31 [s, 3 H, $C(CH_3)_2$ isoprop.], 1.28 (d, 3 H, $J_{6b,5b}$ 6.1 Hz, CH_3), 0.61–0.58 [m, 12 H, $CH(CH_3)_2$ thexyl, $SiC(CH_3)_2$], −0.05 and −0.13 [2 s, 6 H, $Si(CH_3)_2$]. ^{13}C NMR (150.86 MHz, $CDCl_3$): δ 100.61 (d, C-1c), 97.46 (d, C-1b), 96.17 (d, C-1a), 77.50 (d, C-3c), 76.44 (d, C-2a), 75.31 (d, C-4a), 74.71 (d, C-3a), 73.50 (2 d, C-2c,4c), 73.45 (d, C-5a), 72.60 (d, C-2b), 72.07 (2 d, C-4b,5c), 70.24 (d, C-3b), 64.38 (d, C-5b), 62.74 (t, C-6c), 62.61 (t, C-6a), 16.14 (q, C-6b). Anal. Calcd for $C_{68}H_{80}O_{21}Si$: C, 64.69; H, 6.34. Found: C, 64.82; H, 6.58.

Thexyldimethylsilyl (2,6-di-O-benzoyl-β-D-galactopyranosyl)-(1 → 4)-[(3,4-di-O-acetyl-2-O-benzyl-α-L-fucopyranosyl)-(1 → 3)]-2,6-di-O-benzoyl-β-D-glucopyranoside (**21**).—To a soln of **20** (940 mg, 0.745 mmol) at room temperature in dry CH_2Cl_2 (20 mL) were added EtSH (278 mg, 4.47 mmol) and *p*-TsOH · H_2O (24 mg, 0.126 mmol). After stirring for 7 h, the mixture was neutralized with Et_3N and the solvent evaporated. The thioacetal was first removed under high vacuum (1 h). Ensuing flash chromatography (8:2 toluene–acetone) afforded **21** (839 mg, 92%) as an amorphous mass. TLC (8:2 toluene–acetone), R_f 0.26; $[\alpha]_D^{20}$ −14.8° (*c* 1.0, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 8.08–6.88 (m, 25 H, 5 C_6H_5CO), 5.39–5.24 (m, 5 H, H-2a,1b,4b,3b,2c), 5.03 (m, 1 H, H-5b), 4.94–4.86 (m, 1 H, H-6c), 4.71 (d, 1 H, $J_{1a,2a}$ 7.4 Hz, H-1a), 4.66–4.60 (m, 3 H, H-1c ($J_{1c,2c}$ 8.1 Hz), H-6c,6a), 4.44 (dd, 1 H, J_{gem} 11.5, $J_{6a,5a}$ 4.5 Hz, H-6a), 4.34 (d, 1 H, J_{gem} 12.3 Hz, 1/2 CH_2Ph), 4.17 (dd, 1 H, $J_{3a,2a} = J_{3a,4a} = 9.3$ Hz, H-3a), 4.13 (dd, 1 H, $J_{3a,4a} = J_{4a,5a} = 9.3$ Hz, H-4a), 4.03 (d, 1 H, J_{gem} 12.3 Hz, 1/2 CH_2Ph), 3.96 (bs, 1 H, H-4c), 3.70–3.58 (m, 4 H, H-3c,2b,5c,5a), 3.46 (bs, 1 H, OH exch. with D_2O), 2.74 (bs, 1 H, OH exch. with D_2O), 2.00 and 1.82 (2 s, 6 H, 2 CH_3CO), 1.40–1.38 [m, 1 H, $HC(CH_3)_2$ thexyl], 1.25 (d, 3 H, $J_{6b,5b}$ 6.5 Hz, CH_3), 0.63–0.59 [m, 12 H, $CH(CH_3)_2$ thexyl, $SiC(CH_3)_2$), −0.01 and −0.10 [2 s, 6 H, $Si(CH_3)_2$]. ^{13}C NMR (150.86 MHz, $CDCl_3$): δ 100.32 (d, C-1c), 97.05 (d, C-1b), 96.16 (d, C-1a), 76.43 (d, C-2a), 74.24 (d, C-3a), 74.01 (d, C-4a), 73.66 (d, C-2c), 73.47 (d, C-5a), 72.66 (d, C-5c), 72.56 (d, C-3c), 72.11 (d, C-2b), 71.91 (d, C-4b), 70.60 (d, C-3b), 68.14 (d, C-4c), 64.49 (d, C-5b), 62.81 (t, C-6a), 61.84 (t, C-6c), 15.91 (q, C-6b). Anal. Calcd for $C_{65}H_{76}O_{21}Si$: C, 63.91; H, 6.27. Found: C, 63.68; H, 6.22.

Thexyldimethylsilyl (4-O-acetyl-2,6-di-O-benzoyl-β-D-galactopyranosyl)-(1 → 4)-[(3,4-di-O-acetyl-2-O-

benzyl-α-L-fucopyranosyl)-(1 → 3)]-2,6-di-O-benzoyl-β-D-glucopyranoside (**22**).—To a soln of **21** (689 mg, 0.564 mmol) in CH_3CN (6 mL) at room temperature were added $CH_3C(OCH_3)_3$ (203 mg, 1.692 mmol) and a catalytic amount of *p*-TsOH · H_2O. The mixture was stirred for 10 min, then a 80% aq soln of HOAc (9 mL) was added. After stirring for 15 min, the mixture was dild with CH_2Cl_2 (100 mL) and washed with a satd aq soln of $NaHCO_3$ (2 × 80 mL) and H_2O (80 mL). After drying ($MgSO_4$) and evaporation of the solvent, flash chromatography (8:2 toluene–acetone) gave **22** (700 mg, 98%) as an amorphous mass. TLC (3:1 toluene–acetone): R_f 0.47; $[\alpha]_D^{20}$ −26.6° (*c* 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.12–6.84 (m, 25 H, 5 C_6H_5CO), 5.42–5.40 (m, 2 H, H-4c,4b), 5.36 (d, 1 H, $J_{1b,2b}$ 3.8 Hz, H-1b), 5.34 (dd, 1 H, $J_{1a,2a}$ 7.8, $J_{2a,3a}$ 9.5 Hz, H-2a), 5.26 (dd, 1 H, $J_{2b,3b}$ 10.5, $J_{3b,4b}$ 3.2 Hz, H-3b), 5.23 (dd, 1 H, $J_{1c,2c}$ 8.1, $J_{2c,3c}$ 9.5 Hz, H-2c), 5.19–5.10 (m, 1 H, H-5b), 4.75 (dd, 1 H, J_{gem} 11.8, $J_{6c,5c}$ 7.8 Hz, H-6c), 4.76–4.67 (m, 1 H, H-6c), 4.69 (d, 1 H, $J_{1a,2a}$ 7.8 Hz, H-1a), 4.67 (d, 1 H, $J_{1c,2c}$ 8.1 Hz, H-1c), 4.66–4.56 (m, 1 H, H-6a), 4.44 (dd, 1 H, J_{gem} 11.8, $J_{6a,5a}$ 5.0 Hz, H-6a), 4.32 (d, 1 H, J_{gem} 12.4 Hz, 1/2 CH_2Ph), 4.18 (dd, 1 H, $J_{3a,2a} = J_{3a,4a} = 9.5$ Hz, H-3a), 4.04 (dd, 1 H, $J_{4a,5a}$ 9.5 Hz, H-4a), 4.01 (d, 1 H, 1/2 CH_2Ph), 3.94 (m, 1 H, H-3c), 3.84–3.75 (m, 1 H, H-5c), 3.65 (dd, 1 H, $J_{2b,1b}$ 3.8, $J_{2b,3b}$ 10.5 Hz, H-2b), 3.60–3.54 (m, 1 H, H-5a), 2.23, 2.01 and 1.78 (3 s, 9 H, 3 CH_3CO), 1.40–1.36 [m, 1 H, $HC(CH_3)_2$ thexyl), 1.29 (d, 3 H, $J_{6b,5b}$ 6.5 Hz, CH_3), 0.62–0.59 [m, 12 H, $CH(CH_3)_2$ thexyl, $SiC(CH_3)_2$], −0.03 and −0.11 [2 s, 6 H, $Si(CH_3)_2$]; ^{13}C NMR (150.86 MHz, $CDCl_3$): δ 100.66 (d, C-1c), 97.47 (d, C-1b), 96.15 (d, C-1a), 76.30 (d, C-2a), 74.78 (d, C-4a), 74.61 (d, C-3a), 73.41 (d, C-5a), 72.78 (d, C-2c), 72.19 (d, C-2b), 71.91 (d, C-4b), 71.62 (d, C-5c), 71.51 (d, C-3c), 70.45 (d, C-3b), 69.52 (d, C-4c), 64.13 (d, C-5b), 62.60 (t, C-6a), 61.27 (t, C-6c), 15.99 (q, C-6b). Anal. Calcd for $C_{67}H_{78}O_{22}Si$: C, 63.99; H, 6.22. Found: C, 63.72; H, 6.23.

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