Solid-Phase Synthesis of Lactose-Containing Oligosaccharides

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Dedicated to Professor Gérard Descotes in honor of his scientific contributions to carbohydrate chemistry

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The new lactosyl donor **8**, bearing an Fmoc-protected hydroxy group, has been prepared from lactose for the solid-phase synthesis of lactose-containing oligosaccharides. In addition to the preparation of 3b-*O*-fucosyllactoside **1** (with donor **4**), use of this new building block has permitted the syntheses of 3b-*O*-mannosyllactoside **2** and of human milk oligosaccharide lacto-*N*-tetraoside **3**, with known donors **5** and **6**, respectively. These successful, high-yielding syntheses demonstrate the usefulness of Fmoc-protected *O*-glycosyl trichloroacetimidate **8** for the solid-phase construction of oligosaccharides, by an ester-type linker strategy.

Introduction

Polymer-supported syntheses of oligosaccharides have attracted considerable interest over the last few years, and the progress in this field has recently been highlighted in several reviews.[1,2] The solid-phase construction of oligosaccharides presents several advantages over solution-phase synthesis, such as better yields due to the use of excess reagent, and faster syntheses with simpler purification procedures. This technique therefore appears very attractive for applications in combinatorial chemistry and future automation. Efficient solid-phase oligosaccharide synthesis requires a linker stable to all reaction conditions all along the synthesis and allowing the release of the oligosaccharide in high yield. It is also very important to have a successful, high-yielding and stereoselective glycosylation strategy. Our group[3] and others[4,5] have already demonstrated the efficiency of the well-known *O*-glycosyl trichloroacetimidate[6,7] donors for solid-phase oligosaccharide synthesis (SPOS). In this strategy, elongation of the oligosaccharide chain is most often carried out by using the acetyl group as a temporary hydroxy protecting group. Recently, we have reported the efficient preparation and the high promise of *O*-glycosyl trichloroacetimidates bearing Fmoc-protected (Fmoc: 9-fluorenylmethyloxycarbonyl) hydroxy groups for the construction of oligosaccharides in solution and in solid-phase systems.[8] Other types of Fmoc-containing glycosyl donors have also been reported recently.[9,10] The Fmoc group, which can be removed under mildly basic conditions, has also proved very suitable for SPOS in combination with a novel ester-type linker,[8,11] which is orthogonal to Fmoc protection. In an endeavour to develop the use of Fmoc-containing *O*-glycosyl trichloroacetimidates in solid-phase systems in conjunction with this new linker, we have prepared oligosaccharides **1**–**3** (Scheme 1).[12] The synthesis of the *O*-lactosyl trichloroacetimidate donor **8**, bearing an Fmoc group in the 3b-*O*-position, will be described first. This building block was used in conjunction with spacer-connected resin **9**[8] for the preparation of key lactosyl-loaded resin **7**, which should permit elongation with glycosyl donors **4**–**6** at the 3b-*O*-position, to produce carbohydrate moieties of glycosphingolipids.

Results and Discussion

The di-*O*-allylated derivative **10**[13] was prepared from lactose in four steps, using a strategy based on a dibutyltin oxide assisted regioselective allylation of the 3b-*O*-position, as developed by Veyrières and al.[14] (Scheme 2). Subsequent perbenzylation under standard conditions furnished compound **11** in 76% yield. The two allyl groups were removed according to a two-step, ''one-pot'' procedure. Firstly, an isomerization step was carried out using Wilkinson catalyst and 1,8-diaza[5.4.0]bicycloundec-7-ene (DBU) in a mixture of EtOH/toluene/water (8:3:1). The second step, consisting of the hydrolysis of the enol ethers, was performed by treatment with a mixture of HCl and acetone, furnishing the diol **12** in 83% yield.

Next, the regioselective protection of the anomeric position with a thexyldimethylsilyl (TDS) group was successfully accomplished, using 1.15 equiv. of TDS-Cl and 2 equiv. of imidazole in CH_2Cl_2. The monosilylated compound **13** was obtained in 86% yield. The Fmoc group was subsequently introduced by treatment with Fmoc-Cl and catalytic amounts of 4-(dimethylamino)pyridine (DMAP) in pyridine at room temperature, to afford the derivative **14** in 91% yield. The desilylation step was performed with an excess of HF·pyridine complex in THF at room temperature,[15] to furnish the desired compound **15** as an anomeric mixture (1:1) in 93% yield. The trichloroacetimidate

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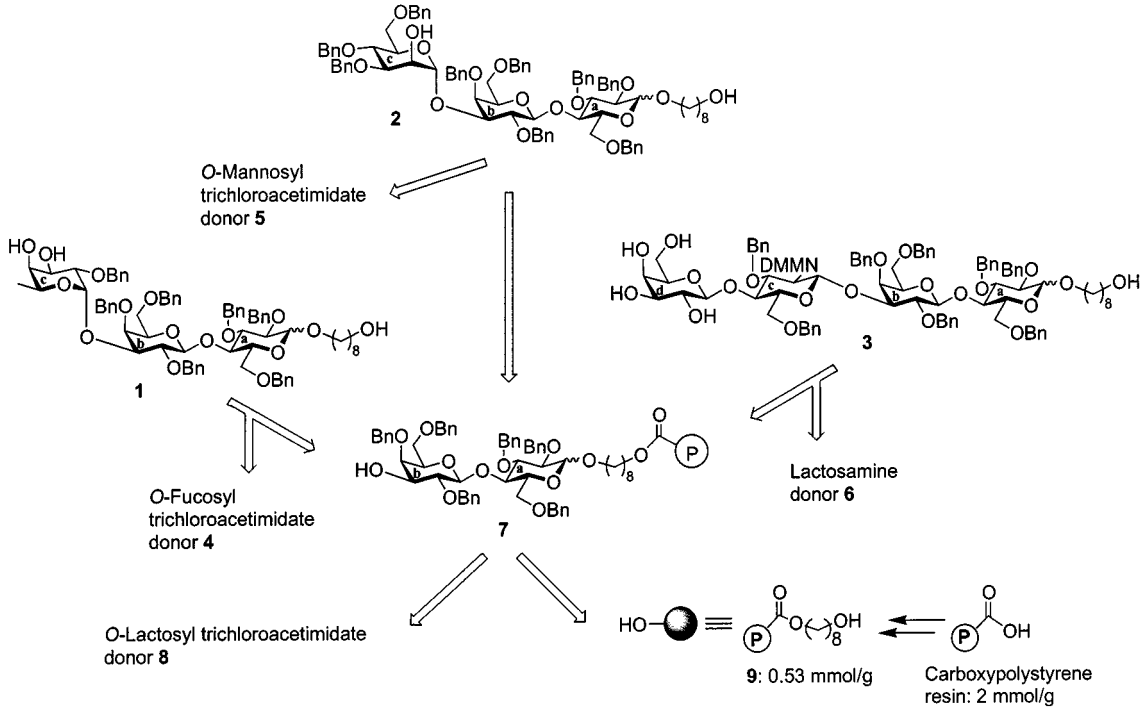
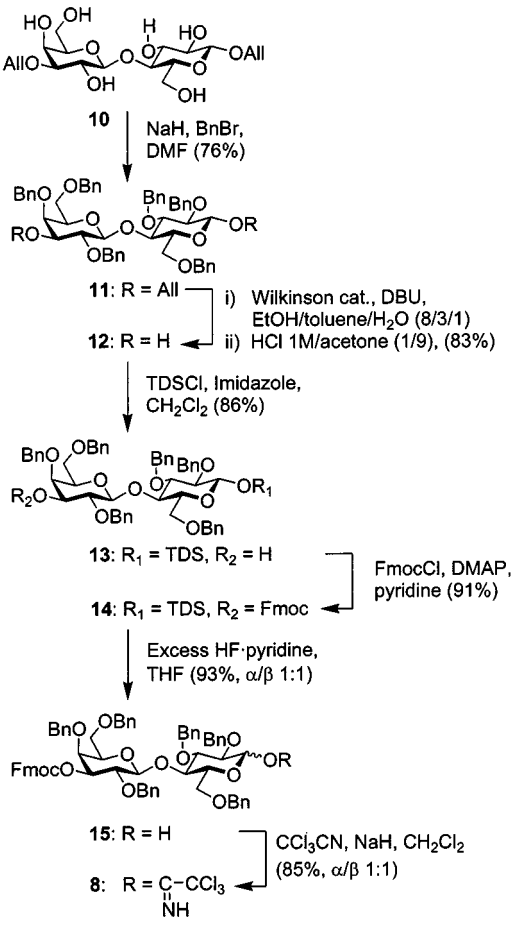


Scheme 1. Building blocks for the synthesis of oligosaccharides **1**, **2** and **3**



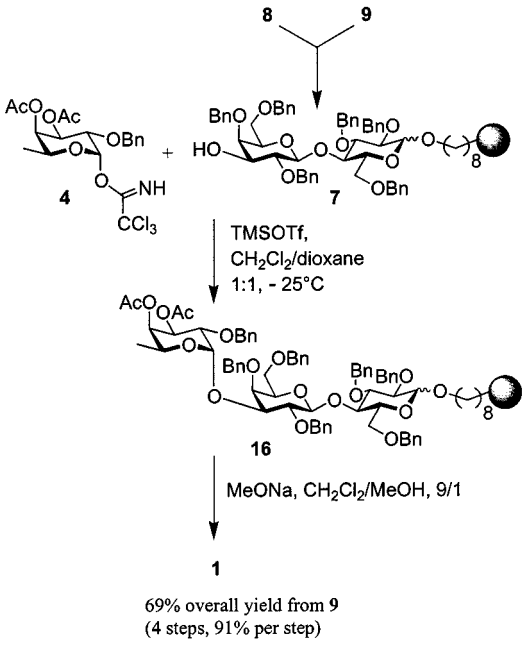
Scheme 2. Synthesis of lactosyl donor **8**

function was introduced under the conditions previously employed,[8] using the minimum required amount of NaH in a mixture of dichloromethane and trichloroacetonitrile (1:1). The *O*-lactosyl trichloroacetimidate **8** was obtained in 85% yield (α/β = 1:1).

Synthesis of Oligosaccharides 1, 2 and 3

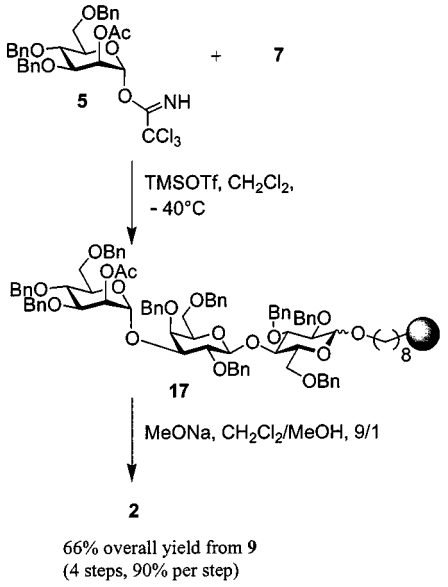
Lactosyl donor **8** was subsequently used for a glycosylation of linker-loaded polystyrene resin **9** (loading of 0.53 mmol/g calculated by colourimetric assay) under trimethylsilyl triflate (TMSOTf) activation as previously described[8] (Scheme 3). After removal of the Fmoc group in the presence of triethylamine in CH_2Cl_2, the obtained lactosyl-loaded resin **7** was subjected to a glycosylation step with 3 equiv. of known fucosyl donor **4**,[16,17] using the previously described experimental conditions [0.3 equiv. of TMSOTf, CH_2Cl_2/dioxane (1:1), −25 °C].[3d] This exclusively yielded an α-anomeric linkage in the resin-bound trisaccharide **16**. This procedure was performed twice to ensure complete 3b-*O*-fucosylation. Reaction completion here and in the next steps was monitored by TLC and MALDI-TOF mass-spectrometric analysis (TLC and MALDI-TOF analysis indicated complete disappearance of the corresponding starting material) of the crude cleavage product (MeONa, CH_2Cl_2/MeOH) from a very small resin sample (2 mg). The final cleavage step under alkaline conditions [5 equiv. MeONa, CH_2Cl_2/MeOH (9:1), 6 h, room temp.] was carried out twice to furnish an anomeric mixture (β/α = 6:4) of 3b-*O*-fucosyl-lactoside **1** in 69% overall yield from **9** (91% per step, 4 steps).

The same procedure was applied to the glycosylation of the key resin **7** with *O*-mannosyl trichloroacetimidate donor



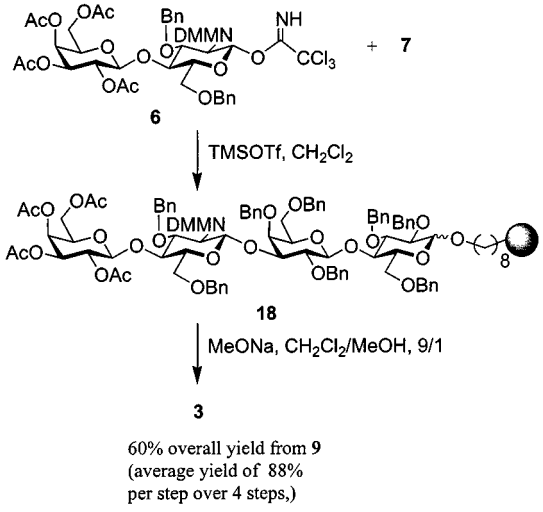
Scheme 3. Synthesis of trisaccharide **1** on solid phase

5.[18,19] This compound was activated with TMSOTf (0.45 equiv.) at −40 °C in dichloromethane to furnish the resin-bound trisaccharide **17**; orthoester formation was not observed under these conditions. Complete 3b-*O*-mannosylation was ensured by performing the procedure twice. Cleavage from the solid support was carried out under the conditions described above to furnish an anomeric mixture (β/α = 6:4) of deacetylated trisaccharide **2** in 66% overall yield from **9** (average yield of 90% per step over 4 steps, Scheme 4).



Scheme 4. Synthesis of trisaccharide **2** on polymer support

Finally, the usefulness of the resin-bound disaccharide **7** was demonstrated with the construction of a human milk oligosaccharide, namely lacto-*N*-tetraose derivative **3**. The recently introduced DMM-protected (DMM: dimethylmaleoyl)[20] lactosamine donor **6**,[21] already successfully used in solid-phase systems,[3a] was selected for this task (Scheme 5). To this end, 3 equiv. of **6** were treated with resin **7** under TMSOTf activation conditions (0.3 equiv.) in CH_2Cl_2 at room temperature. This glycosylation step was carried out twice to ensure complete disappearance of the disaccharide. The obtained resin-bound tetrasaccharide **18** was then cleaved from the polymer support under alkaline conditions to afford, after purification by flash chromatography, the lacto-*N*-tetraose derivative **3** as an anomeric mixture (β/α = 6:4) in 60% overall yield over 4 steps from **9** (88% per step). Structural assignments of the newly generated α-fucosyl anomeric linkage of **1**, the α-mannosyl anomeric linkage of **2**, and the β-lactosamine anomeric linkage of **3** are based on the NMR-spectroscopic data, for instance, ^{1}H NMR: 1c-H: **1**, $J_{1,2} \approx 4$ Hz; **2**, $J_{1,2} < 1$ Hz; **3**, $J_{1,2} \approx 8$ Hz; ^{13}C NMR: 1c-C: **1**, δ = 97.2; **2**, δ = 95.4; **3**, δ = 100.3.



Scheme 5. Synthesis of lacto-*N*-tetraose derivative **3** on solid phase

Conclusion

The usefulness of Fmoc protection in SPOS was demonstrated with newly prepared *O*-lactosyl trichloroacetimidate **8**. Application of this lactosyl donor to the construction of oligosaccharides in a solid-phase system, using a simple ester-type linker, gave highly promising results. In addition to the synthesis of the trisaccharide **1**, two new tri/tetrasaccharides, namely **2** and **3**, were prepared in excellent overall yields. Thus, the stability of Fmoc protection under the glycosylation conditions and the selective removal of the Fmoc protecting group in the presence of the ester-type linker was confirmed. These results should constitute a basis for the preparation of combinatorial libraries of oligosaccharides

based on polymer-bound lactoside **7**. Investigations along these lines are currently underway.

Experimental Section

General Remarks: Solvents were purified and dried in the usual way. All reactions were performed with dry solvents and under argon unless otherwise stated. − TLC was performed on silica gel 60 F_{254} plastic plates. − Detection was achieved by treatment with a solution of 20 g of ammonium molybdate and 0.4 g of cerium(IV) sulfate in 400 mL of 10% H_2SO_4 or with 15% H_2SO_4, and heating at 150 °C. − Flash chromatography was carried out on silica gel (Baker 30−60 μm). Adsorption of crude reaction products was performed using silica gel (Baker 60−200 μm). Petroleum ether used was of the boiling range 35−70 °C; toluene, CH_2Cl_2, MeOH and EtOAc were distilled. − Optical rotations were determined at 21 °C with a Perkin−Elmer 241/MC polarimeter (1-dm cell). − NMR spectra were recorded with Bruker AC 250 and 600 DRX instruments, with tetramethylsilane as internal standard. − Mass spectra were recorded with a MALDI-kompakt (Kratos) instrument in the positive mode using 2,5-dihydroxybenzoic acid in THF as matrix. − Microanalyses were performed in the Microanalysis Unit at the Fachbereich Chemie, Universität Konstanz.

Allyl *O*-(3-*O*-Allyl-2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (11): Dry NaH (95% in oil, 2.5 equiv. per OH, 4.2 g, 167.1 mmol) was added at 0 °C to a mixture of **10** (4.70 g, 11.1 mmol) and benzyl bromide (2.2 equiv. per OH, 17.5 mL, 147.0 mmol) in DMF (100 mL). The reaction mixture was allowed to warm to room temp. and was stirred for 20 h under argon. The reaction was quenched by careful addition of methanol and the solvents were evaporated in vacuo. The residue was diluted in diethyl ether and the organic phase was washed with water and brine, dried with $MgSO_4$ and concentrated in vacuo. The crude residue was purified by flash chromatography (toluene/ethyl acetate, 95:5) to furnish **11** (8.15 g, 8.46 mmol) as a colourless oil in 76% yield. − TLC (toluene/EtOAc, 9:1): R_f = 0.5. − ^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.22 (dd, $^3J_{2,3}$ = 9.7, $^3J_{3,4}$ = 2.8 Hz, 1 H, 3b-H), 3.25−3.30 (m, 3 H, 5a-H, 5b-H, 6b-H), 3.35 (dd, $^3J_{1,2}$ = $^3J_{2,3}$ = 8.1 Hz, 1 H, 2a-H), 3.44−3.49 (m, 2 H, 6′b-H, 3a-H), 3.60−3.70 (m, 3 H, 2b-H, 6a-H, 6′a-H), 3.79 (m, 1 H, 4b-H), 3.84 (dd, $^3J_{2,3}$ = $^3J_{3,4}$ = 9.3 Hz, 1 H, 4a-H), 4.04−4.12 (m, 3 H, 3 × C*H*HCH=CH_2), 4.16 (d, 1 H, J_{AB} = 11.7 Hz, PhC*H*H), 4.25 (d, 1 H, J_{AB} = 11.7 Hz, PhC*H*H), 4.31−4.36 (m, 4 H, C*H*HCH=CH_2, 3 × PhC*H*H), 4.44−4.47 (m, 2 H, 2 × PhC*H*H), 4.63−4.66 (m, 3 H, 3 × PhC*H*H), 4.71 (d, 1 H, J_{AB} = 11.1 Hz, PhC*H*H), 4.82 (d, 1 H, J_{AB} = 10.9 Hz, PhC*H*H), 4.87 (d, 1 H, J_{AB} = 11.4 Hz, PhC*H*H), 4.93 (d, 1 H, J_{AB} = 10.7 Hz, PhC*H*H), 5.08−5.12 (m, 2 H, 2 × CH_2CH=C*H*H), 5.22−5.27 (m, 2 H, 2 × CH_2CH=C*H*H), 5.80−5.92 (m, 2 H, 2 × CH_2C*H*=CH_2), 7.01−7.29 (m, 30 H, 6 × Ph). − ^{13}C NMR (150.9 MHz, $CDCl_3$): δ = 68.0 (6b-C), 68.4 (6a-C), 70.2, 71.4 (2 C, 2 × OAll), 72.9 (5b-C), 73.0, 73.4 (2 s, 3C, *C*H_2Ph), 73.5 (4b-C), 74.6, 75.2 (2 s, 3 C, *C*H_2Ph), 75.2 (5a-C), 76.8 (4a-C), 79.9 (2b-C), 81.7 (2a-C), 82.4 (3b-C), 82.9 (3a-C), 102.6, 102.7 (1a-C, 1b-C). − MALDI-MS; *m*/*z*: 986.4 [M + Na^+]. − $C_{60}H_{66}O_{11}$ (963.19): calcd. C 74.82, H 6.91; found C 74.94, H 7.02.

***O*-(2,4,6-Tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α/β-D-glucopyranose (12):** A mixture of **11** (3.97 g, 4.12 mmol), Wilkinson's catalyst (0.1 equiv., 0.38 g, 0.41 mmol) and DBU (0.1 equiv., 0.06 mL, 0.41 mmol) in EtOH/toluene/water (8:3:1, 45 mL) was refluxed for 24 h. Solvents were evaporated and the residue was diluted in Et_2O (200 mL). The organic phase was washed with water and brine, and the solvents were removed in vacuo. The residue was dissolved in an acetone/HCl (1 M) mixture (9:1, 45 mL) and the reaction was stirred for 2 h at room temp. The solvents were subsequently removed in vacuo and the residue was diluted in Et_2O. The organic layer was washed successively with saturated aqueous $NaHCO_3$ solution and water and dried with $MgSO_4$, and the solvents were removed in vacuo. The residue was adsorbed onto silica gel in toluene and purified by flash chromatography (petroleum ether/EtOAc, 7:3) to give **12** (3.01 g, 3.41 mmol) as a gum (α/β = 1:1) in 83% yield. − TLC (petroleum ether/EtOAc, 7:3): R_f = 0.18. − ^{1}H NMR (600 MHz, $CDCl_3$): α anomer: δ (selected data) = 2.08 [d, 1 H, OH (3b)], 2.93 [s, 1 H, OH (1a)], 3.25 (dd, $^3J_{2,3}$ = $^3J_{1,2}$ = 8.2 Hz, 1 H, 2a-H), 3.30−3.56 (m, 7 H, 3b-H, 5b-H, 2b-H, 6b-H, 2a-H, 6a-H, 6′b-H), 3.72−3.81 (m, 3 H, 4b-H, 3a-H, 6′a-H), 3.85−4.00 (m, 2 H, 4a-H, 5a-H), 4.27 (d, $^3J_{1,2}$ = 7.3 Hz, 1 H, 1b-H), 5.10 (d, $^3J_{1,2}$ = 3.7 Hz, 1 H, 1a-H); β anomer: δ (selected data) = 2.09 [d, 1 H, OH (3b)], 3.09 [m, 1 H, OH (1a)], 3.25 (dd, $^3J_{2,3}$ = $^3J_{1,2}$ = 8.2 Hz, 1 H, 2a-H), 3.31−3.56 (m, 6 H, 3b-H, 5a-H, 5b-H, 6b-H, 3a-H, 6′b-H), 3.63 (m, 1 H, 6a-H), 3.69 (dd, 1 H, $^2J_{6,6'}$ = 10.7 Hz, $^3J_{5,6'}$ = 4.3 Hz, 6′a-H), 3.75 (m, 1 H, 4b-H), 3.89 (m, 1 H, 4a-H), 4.27 (d, $^3J_{1,2}$ = 7.3 Hz, 1 H, 1b-H), 4.61 (d, 1 H, 1a-H). − ^{13}C NMR (150.9 MHz, $CDCl_3$): α anomer: δ (selected data) = 68.3 (s, 2 C, 6a-C, 6b-C), 70.8 (5a-C), 73.7 (3b-C), 74.4 (5b-C), 76.2 (4b-C), 76.9 (4a-C), 79.5 (2a-C), 80.2 (3a-C), 80.9 (2b-C), 91.8 (1a-C), 103.1 (1b-C); β anomer: δ (selected data) = 68.3 (6b-C), 68.8 (6a-C), 73.7 (3b-C), 74.4 (5b-C), 75.5 (5a-C), 76.2 (4b-C), 76.9 (4a-C), 80.9 (2b-C), 83.0 (2a-C), 83.1 (3a-C), 97.8 (1a-C), 103.1 (1b-C). − MALDI-MS; m/z: 905.7 [M + Na^+]. − $C_{54}H_{58}O_{11}$ (883.06): calcd. C 73.45, H 6.62; found C 73.29 H 6.69.

Thexyldimethylsilyl (2,4,6-Tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (13): TDS-Cl (1.15 equiv., 0.90 mL, 4.55 mmol) and imidazole (2 equiv., 0.54 g, 7.92 mmol) were added under argon to a solution of diol **12** (3.50 g, 3.96 mmol) in dichloromethane. The reaction mixture was stirred for 16 h (complete consumption of the starting material by TLC) and the solvent was then evaporated in vacuo. The residue was adsorbed onto silica gel in toluene and purified by flash chromatography (petroleum ether/EtOAc, 8:2) to afford **13** (3.49 g, 3.40 mmol) as a gum in 86% yield. − TLC (petroleum ether/EtOAc, 7:3): R_f = 0.5. − $[\alpha]_D$ = +5.7 (*c* = 1.03, chloroform) − ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.15 [s, 3 H, Si(CH_3)$_2$], 0.18 [s, 3 H, Si(CH_3)$_2$], 0.87 [m, 12 H, C(CH_3)$_2$ thexyl, SiC(CH_3)$_2$], 1.62−1.72 [m, 1 H, C*H*(CH_3)$_2$ thexyl], 2.16 (d, 1 H, $^3J_{H,OH}$ = 5.7 Hz, O*H*), 3.31−3.34 (m, 2 H, 2a-H, 5b-H), 3.39 (dd, 1 H, $^2J_{6,6'}$ = 8.8, $^3J_{5,6}$ = 5.1 Hz, 6a-H), 3.43−3.58 (m, 5 H, 5a-H, 2b-H, 4a-H, 3b-H, 6′a-H), 3.66 (dd, 1 H, 6b-H), 3.78 (dd, 1 H, $^2J_{6,6'}$ = 10.9, $^3J_{5,6}$ = 3.9 Hz, 6′b-H), 3.84 (m, 1 H, 4b-H), 3.96 (dd, $^3J_{2,3}$ = $^3J_{3,4}$ = 9.4 Hz, 1 H, 3a-H), 4.25 (d, 1 H, J_{AB} = 11.8 Hz, PhC*H*H), 4.37 (d, 1 H, J_{AB} = 11.8 Hz, PhC*H*H), 4.43−4.48 (m, 2 H, 1b-H, PhC*H*H), 4.53−4.63 (m, 3 H, 1a-H, 2 × PhC*H*H), 4.65−4.77 (m, 4 H, 4 × PhC*H*H), 4.80 (d, 1 H, J_{AB} = 11.5 Hz, PhC*H*H), 4.88 (d, 1 H, J_{AB} = 10.9 Hz, PhC*H*H), 5.01 (d, 1 H, J_{AB} = 10.7 Hz, PhC*H*H), 7.08−7.37 (m, 30 H, 6 × Ph). − ^{13}C NMR (150.9 MHz, $CDCl_3$): δ = −3.0, −1.9 [2 s, 2C, Si(CH_3)$_2$], 18.4, 18.6, 19.9, 20.1 [4 s, 4C, C(CH_3)$_2$ thexyl, SiC(CH_3)$_2$], 33.8 [C*H*(CH_3)$_2$ thexyl], 68.0 (6a-C), 68.4 (6b-C), 73.2 (*C*H_2Ph), 73.3 (s, 2C, 5a-C, *C*H_2Ph), 74.1 (3b-C), 74.9 (*C*H_2Ph), 75.0 (s, 2C, 2*C*H_2Ph), 75.1 (*C*H_2Ph), 75.2 (5b-C), 75.9 (4b-C), 76.7 (3a-C), 80.7 (2b-C), 83.0 (4a-C), 83.7 (2a-C), 98.1 (1a-C), 102.7 (1b-C), 127.0, 127.4, 127.5, 127.6, 127.7, 127.9, 128.0, 128.2, 128.3, 128.4 (10 s, 30 C, *C*HAr), 138.0, 138.3, 138.4, 138.7, 139.2 (5 s, 6 C, C_{ipso}). − MALDI-MS; *m*/*z*: 1048.3 [M

+ Na^+]. − $C_{62}H_{76}O_{11}Si$ (1025.38): calcd. C 72.63, H 7.47; found C 72.34. H 7.38.

Thexyldimethylsilyl (2,4,6-Tri-*O*-benzyl-3-*O*-(9-fluorenylmethoxycarbonyl)-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (14): Fmoc-Cl (4 equiv., 4.08 g, 15.8 mmol) and DMAP (0.1 equiv., 48.2 mg, 0.39 mmol) were added under argon to a solution of **13** (4.05 g, 3.95 mmol) in pyridine. The yellow solution was stirred for 3 h (complete disappearance of the starting material by TLC) and the solvent was then evaporated and coevaporated three times with toluene in vacuo. The crude residue was adsorbed onto silica gel in toluene and purified by flash chromatography (petroleum ether/EtOAc, 89:11) to furnish **14** (4.81 g, 3.59 mmol) as a white foam in 91% yield. − TLC (petroleum ether/EtOAc, 85:15): R_f = 0.45. − $[\alpha]_D$ = +12.2 (*c* = 0.54, chloroform) − ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.15 [s, 3 H, $Si(CH_3)_2$], 0.18 [s, 3 H, $Si(CH_3)_2$], 0.87 [m, 12 H, $C(CH_3)_2$ thexyl, $SiC(CH_3)_2$], 1.63−1.71 (m, 1 H, $CH(CH_3)_2$ thexyl), 3.25−3.37 (m, 3 H, 2a-H, 5a-H, 6b-H), 3.44−3.55 (m, 3 H, 5b-H, 3a-H, 6′b-H), 3.62 (m, 1 H, 6a-H), 3.73−3.81 (m, 2 H, 2b-H, 6′a-H), 3.92−3.99 (m, 2 H, 4a-H, 4b-H), 4.17−4.26 [m, 2 H, PhC*H*H, 9-H (Fmoc)], 4.33−4.39 [m, 3 H, PhC*H*H, CH_2O (Fmoc)], 4.40−4.45 (m, 2 H, 2 × PhC*H*H), 4.49−4.54 (m, 2 H, 1b-H, PhC*H*H), 4.61 (d, $^3J_{1,2}$ = 7.5 Hz, 1 H, 1a-H), 4.63−4.78 (m, 7 H, 3b-H, 6 × PhC*H*H), 4.88 (d, 1 H, J_{AB} = 10.9 Hz, PhC*H*H), 4.97 (d, 1 H, J_{AB} = 10.7 Hz, PhC*H*H), 7.08−7.42 (m, 34 H, Ph), 7.54−7.57 [m, 2 H, Ph (Fmoc)], 7.69−7.73 [m, 2 H, Ph (Fmoc)]. − ^{13}C NMR (150.9 MHz, $CDCl_3$): δ = −3.0, −1.9 [2 s, 2 C, $Si(CH_3)_2$], 18.5, 18.7, 19.9, 20.1 [4 s, 4 C, $C(CH_3)_2$ thexyl, $SiC(CH_3)_2$], 33.9 [*C*H$(CH_3)_2$ thexyl], 46.6 [9-C (Fmoc)], 67.5 (6b-C), 68.2 (6a-C), 69.6 [CH_2O (Fmoc)], 72.6 (5b-C), 73.1 (CH_2Ph), 73.3 (s, 2 C, 2 × CH_2Ph), 74.1 (4b-C), 74.9 (5a-C), 75.1 (s, 2 C, 2 × CH_2Ph), 75.2 (CH_2Ph), 76.7 (4a-C), 77.7 (2b-C), 79.6 (3b-C), 82.8 (3a-C), 83.6 (2a-C), 98.1 (1a-C), 102.4 (1b-C), 120.0, 125.1, 127.0, 127.1, 127.4, 127.6, 127.7, 127.9, 128.0, 128.2 (11 s, 38 C, *C*HAr), 138.3, 138.7, 139.2, 141.3, 143.1, 143.4 (6 s, 10 C, C_{ipso}), 154.6 [O*C*=OO (Fmoc)]. − MALDI-MS; *m*/*z*: 1270.9 [M + Na^+]. − $C_{77}H_{86}O_{13}Si$ (1247.62): calcd. C 74.13, H 6.95; found C 74.08. H 7.06.

***O*-(2,4,6-Tri-*O*-benzyl-3-*O*-(9-fluorenylmethoxycarbonyl)-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α/β-D-glucopyranose (15):** An excess of HF·pyridine complex (7 mL) was added under argon to a solution of **14** (4.78 g, 3.83 mmol) in THF in a Teflon flask. The solution was stirred overnight (complete disappearance of the starting material by TLC) and diluted in Et_2O. The organic solution was then washed with saturated aqueous $NaHCO_3$ solution and water and dried with Na_2SO_4, and the solvents were removed in vacuo. The residue was adsorbed onto silica gel in toluene and purified by flash chromatography (petroleum ether/EtOAc, 7:3) to yield **15** (3.94 g, 3.56 mmol) as a white foam in 93% yield (α/β = 1:1). − TLC (petroleum ether/EtOAc; 7:3): R_f = 0.24. − ^{1}H NMR (600 MHz, $CDCl_3$): α anomer**:** δ = 2.95 (d, 1 H, $^3J_{H1,OH}$ = 1.6 Hz, OH), 3.34−3.43 (m, 2 H, 5b-H, 6b-H), 3.47−3.56 (m, 3 H, 6a-H, 2a-H, 6′b-H), 3.74−3.84 (m, 3 H, 2b-H, 3a-H, 6′a-H), 3.92−3.97 (m, 3 H, 5a-H, 4a-H, 4b-H), 4.19−4.27 [m, 2 H, PhCHH, 9-H (Fmoc)], 4.31−4.47 [m, 5 H, 2 × PhCHH, CH_2O (Fmoc)], 1b-H), 4.53 (d, 1 H, J_{AB} = 12 Hz, PhCHH), 4.63−4.72 (m, 4 H, 3b-H, 3 × PhCHH), 4.74 (d, 1 H, J_{AB} = 11.8 Hz, PhCHH), 4.80 (d, 1 H, J_{AB} = 11.4 Hz, PhCHH), 5.02 (d, 1 H, J_{AB} = 10.7 Hz, PhCHH), 5.16 (m, 1 H, 1a-H), 7.09−7.38 (m, 34 H, Ph), 7.55−7.59 [m, 2 H, Ph (Fmoc)], 7.69−7.74 [m, 2 H, Ph (Fmoc)]; β anomer**:** δ = 3.06 (d, 1 H, $^3J_{H1,OH}$ = 5.9 Hz, OH), 3.28−3.39 (m, 4 H, 5b-H, 6b-H, 2a-H, 5a-H), 3.46−3.57 (m, 3 H, 6a-H, 3a-H, 6′b-H), 3.64 (m, 1 H, 6′b-H), 3.72−3.80 (m, 2 H, 6a-H, 2b-H), 3.93−3.97 (m, 2 H, 4a-H, 4b-H), 4.19−4.27 [m, 2 H, PhCHH, 9-H (Fmoc)], 4.32−4.46 [m, 5 H, 2 × PhCHH, CH_2O (Fmoc), 1b-H], 4.52 (d, 1 H, J_{AB} = 11.9 Hz, PhCHH), 4.61−4.70 (m, 5 H, 3b-H, 1a-H, 3 × PhCHH), 4.76 (d, 1 H, J_{AB} = 11.6 Hz, PhCHH), 4.86 (d, 1 H, J_{AB} = 11.1 Hz, PhCHH), 4.99 (d, 1 H, J_{AB} = 10.7 Hz, PhCHH), 7.09−7.38 (m, 34 H, Ph), 7.55−7.59 [m, 2 H, Ph (Fmoc)], 7.69−7.74 [m, 2 H, Ph (Fmoc)]. − ^{13}C NMR (150.9 MHz, $CDCl_3$): α anomer**:** δ = 46.7 [9-C (Fmoc)], 67.7 (6b-C), 67.8 (6a-C), 69.8 [CH_2O (Fmoc)], 70.4 (5a-C), 72.7 (5b-C), 73.2 (CH_2Ph), 73.3 (CH_2Ph), 73.6 (CH_2Ph), 74.1 (4b-C), 75.0 (s, 2 C, 2 × CH_2Ph), 75.4 (CH_2Ph), 76.4 (4a-C), 77.7 (2b-C), 79.1 (2a-C), 79.7 (3b-C), 79.8 (3a-C), 91.4 (1a-C), 102.5 (1b-C), 120.0, 125.0, 127.1, 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 128.4 (13 s, 38 C, CHAr), 137.8, 138.0, 138.1, 138.3, 138.4, 139.1, 141.2, 141.3 (8 s, 10 C, C_{ipso}), 154.8 [OC=OO (Fmoc)]; β anomer**:** δ = 46.7 [9-C (Fmoc)], 67.7 (6b-C), 68.1 (6a-C), 69.8 [CH_2O (Fmoc)], 72.7 (s, 2 C, 5a-C, 5b-C), 73.2 (CH_2Ph), 73.3 (CH_2Ph), 73.6 (CH_2Ph), 74.1 (4b-C), 75.0 (s, 2 C, 2 × CH_2Ph), 75.4 (s, 2 C, 5a-C, CH_2Ph), 76.4 (4a-C), 77.7 (2b-C), 79.7 (3b-C), 82.8 (s, 2 C, 2a-C, 3a-C), 97.3 (1a-C), 102.5 (1b-C), 120.0, 125.0, 127.1, 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 128.4 (13 s, 38 C, CHAr), 137.8, 138.0, 138.1, 138.3, 138.4, 139.1, 141.2, 141.3 (8 s, 10 C, C_{ipso}), 154.8 [OC=OO (Fmoc)]. − MALDI-MS; *m*/*z*: 1128.3 [M + Na^+]. − $C_{69}H_{68}O_{13}$ (1105.30): calcd. C 74.98, H 6.20; found C 74.89. H 6.37.

***O*-[(2,4,6-Tri-*O*-benzyl-3-*O*-(9-fluorenylmethoxycarbonyl)-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α/β-D-glucopyranosyl] Trichloroacetimidate (8):** Compound **15** (1.01 g, 0.91 mmol) was dissolved in a CH_2Cl_2/CCl_3CN mixture (1:1, 9 mL) under argon. The minimum amount of sodium hydride (95% in oil) required for the completion of the reaction (TLC monitoring) was added to the solution. After 30 min of stirring, the solution was adsorbed onto silica gel and the residue was purified by flash chromatography (petroleum ether/EtOAc; 78:22) to give **8** (0.96 g, 0.77 mmol) as a white foam in 85% yield (α/β = 1:1). − TLC (petroleum ether/EtOAc, 7:3): R_f = 0.31. − ^{1}H NMR (600 MHz, $CDCl_3$): α anomer**:** δ = 3.23−3.50 (m, 4 H, 6b-H, 6′b-H, 5b-H, 6a-H), 3.55−3.63 (m, 3 H, 6′a-H, 2a-H, 3a-H), 3.70 (m, 1 H, 2b-H), 3.81−3.92 (m, 2 H, 5a-H, 4b-H), 4.02 (m, 4a-H), 4.10−4.22 [m, 2 H, PhCHH, 9-H (Fmoc)], 4.23−4.38 [m, 7 H, 4 × PhCHH, CH_2O (Fmoc), 1b-H], 4.49 (d, 1 H, J_{AB} = 12.1 Hz, PhCHH), 4.53−4.73 (m, 5 H, 3b-H, 4 × PhCHH), 4.79 (d, 1 H, J_{AB} = 10.7 Hz, PhCHH), 4.94 (d, 1 H, J_{AB} = 10.7 Hz, PhCHH), 6.34 (d, $^3J_{1,2}$ = 3.3 Hz, 1 H, 1a-H), 6.98−7.30 (m, 34 H, Ph), 7.46−7.51 [m, 2 H, Ph (Fmoc)], 7.62−7.66 [m, 2 H, Ph (Fmoc)], 8.50 (s, 1 H, NH); β anomer**:** δ = 3.33−3.49 (m, 5 H, 6b-H, 6′b-H, 5b-H, 5a-H, 6a-H), 3.60 (m, 1 H, 2a-H), 3.66−3.79 (m, 2 H, 6a-H, 2b-H), 3.81−3.90 (m, 2 H, 3a-H, 4b-H), 4.02 (m, 4a-H), 4.10−4.22 [m, 2 H, PhCHH, 9-H (Fmoc)], 4.23−4.38 [m, 6 H, 4 × PhCHH, CH_2O (Fmoc)], 4.39−4.52 (m, 2 H, 1b-H, PhCHH), 4.53−4.73 (m, 5 H, 3b-H, 4 × PhCHH), 4.79 (d, 1 H, J_{AB} = 10.7 Hz, PhCHH), 4.90 (d, 1 H, J_{AB} = 10.9 Hz, PhCHH), 5.69 (d, $^3J_{1,2}$ = 7.2 Hz, 1 H, 1a-H), 6.98−7.30 (m, 34 H, Ph), 7.46−7.51 [m, 2 H, Ph (Fmoc)], 7.62−7.66 [m, 2 H, Ph (Fmoc)], 8.58 (s, 1 H, NH). − ^{13}C NMR (150.9 MHz, $CDCl_3$): α anomer**:** δ = 46.7 [9-C (Fmoc)], 67.3 (6a-C), 67.5 (6b-C), 69.8 [CH_2O (Fmoc)], 72.6 (5b-C), 73.0 (5a-C), 73.1, 73.3 (2 s, 2 C, 2 × CH_2Ph), 74.0 (4b-C), 75.2, 75.7 (2 s, 3 C, 3 × CH_2Ph), 75.9 (4a-C), 77.0 (CH_2Ph), 77.5 (2b-C), 79.7 (3b-C), 80.2 (2a-C or 3a-C), 82.6 (2a-C or 3a-C), 94.4 (1a-C), 102.4 (1b-C), 120.0, 125.0, 127.1, 127.5, 127.6, 127.7, 127.8, 128.0, 128.1, 128.2, 128.3 (11 s, 38 C, CHAr), 138.0, 138.1, 138.3, 138.8, 138.9, 141.2, 143.0, 143.3 (8 s, 10 C, C_{ipso}), 154.6 [OC=OO (Fmoc)], 160.9 (C=NH). β anomer**:** δ = 46.7 [9-C (Fmoc)], 67.3 (6a-C), 67.5 (6b-C), 69.8 [CH_2O

(Fmoc)], 72.6 (5b-C), 73.1, 73.3 (2 s, 2 C, 2 × CH_2Ph), 74.0 (4b-C), 75.0, 75.3 (2 s, 3 C, 3 × CH_2Ph), 75.8 (5a-C), 75.9 (4a-C), 77.2 (CH_2Ph), 77.5 (2b-C), 78.4 (2a-C), 79.4 (3a-C), 79.6 (3b-C), 98.1 (1a-C), 102.3 (1b-C), 120.0, 125.0, 127.1, 127.5, 127.6, 127.7, 127.8, 128.0, 128.1, 128.2, 128.3 (11 s, 38 C, CHAr), 138.0, 138.1, 138.3, 138.8, 138.9, 141.2, 143.0, 143.3 (8 s, 10 C, C_{ipso}), 154.6 [OC=OO (Fmoc)], 160.3 (C=NH). − $C_{71}H_{68}Cl_3NO_{13}$ (1249.69): calcd. C 68.24, H 5.48, N 1.12; found C 68.30, H 5.38, N 1.17.

Procedure for Calculation of the Loading: Known dry *O*-tritylated resin[8] obtained from linker-loaded resin **9** was swollen in CH_2Cl_2 (0.40 mL/10 mg resin) and the resulting suspension was agitated for 10 min under argon. TFA (20 μL, 5% of the total volume) was added and shaking was continued for 15 min. The resin was then washed with 25 mL of a CH_2Cl_2/TFA (95:5, v/v) solution. UV measurement was then carried out on this solution (calculation of the concentration using a standard straight line prepared with the UV values of TrOH in a solution of 5% TFA in CH_2Cl_2), giving a loading of 0.53 mmol/g.

General Procedure for the Solid-Phase Glycosylation (Procedure A): Dry acceptor-loaded resins were directly swollen under argon in CH_2Cl_2 solutions (1−1.5 mL/0.1 g resin) containing the appropriate donor (3 equiv.). After 10 min under agitation, 0.3 equiv. of a freshly prepared 0.25 M TMSOTf solution in CH_2Cl_2 was added, and shaking was continued for 1 h at room temp. The resin was then filtered off, washed with CH_2Cl_2 (4 × 5 mL) and THF (4 × 5 mL), and dried under high vacuum. This procedure was repeated prior to starting the next step.

General Procedure for Cleavage (Procedure B): Dry resin was swollen in CH_2Cl_2 (1−1.5 mL/0.1 g resin) and the resulting suspension was shaken under argon for 10 min. A solution of 5 equiv. of MeONa in MeOH (10% of the total volume) was added and the resulting mixture was agitated for 6 h under an inert atmosphere. After this period, TLC analysis confirmed satisfactory cleavage. The resin was rinsed off with CH_2Cl_2/MeOH (9:1, 3 × 5 mL). This procedure was repeated to ensure a complete cleavage. Amberlite IR120 resin (H^+ form) was added to the combined filtrate and washings to neutralize the medium and then filtered off. The solution was concentrated in vacuo and the residue purified by flash chromatography. In the case of an analytical cleavage, the crude residue was directly analyzed by TLC and MALDI-TOF.

Resin 9 was prepared according to the procedure previously described.[8]

Resin 7: Linker-loaded resin **9** was glycosylated with **8** using procedure A.

Resin 16: Lactosyl-loaded resin **7** was glycosylated with **4** following Procedure A, but at −25 °C in a CH_2Cl_2/dioxane (1:1) mixture.

Resin 17: Resin-bound disaccharide **7** was glycosylated with **5** following Procedure A, but using 0.45 equiv. of TMSOTf and working at −40 °C.

Resin 18: Lactosyl-loaded resin **7** was glycosylated with **6** using procedure A.

8-Hydroxyoctyl 3-*O*-[(2-*O*-Benzyl-α-L-fucopyranosyl)]-(1→3)-(2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α/β-D-glucopyranoside (1): Compound **1** was obtained following Procedure B. The crude residue was purified by flash chromatography (petroleum ether/EtOAc, 4:6) to afford **1** (17.3 mg, 69% overall yield from resin **9**) as an oil (α/β = 4:6). − TLC (petroleum ether/EtOAc, 2:8): R_f = 0.41. − ^{1}H NMR (600 MHz, $CDCl_3$): α anomer**:** δ (selected data) = 1.26 (3 H, CH_3), 3.34 (5b-H), 3.37 (2a-H), 3.42 (5a-H), 3.62 (3b-H), 3.70 (4b-H), 3.71 (2b-H), 3.86 (4a-H), 4.00 [1 H, PhC*H*H (Fuc)], 4.20 (1b-H), 4.37 [1 H, PhC*H*H (Fuc)], 5.45 ($^3J_{1,2}$ ≈ 4 Hz, 1c-H); β anomer**:** δ (selected data) = 1.26 (3 H, CH_3), 3.10 (5a-H), 3.29 (2a-H), 3.38 (5b-H), 3.39 (3a-H), 3.46 (6a-H), 3.53 (2c-H), 3.64 (6a-H′), 3.66 (4c-H), 3.70 (4b-H), 3.71 (3b-H), 3.73 (2b-H), 3.83 (3c-H), 3.89 (5c-H), 3.90 (4a-H), 4.00 [1 H, PhC*H*H (Fuc)], 4.20 (1a-H), 4.36 (1b-H), 4.37 [1 H, PhC*H*H (Fuc)], 5.45 ($^3J_{1,2}$ ≈ 4 Hz, 1c-H). − ^{13}C NMR (150.9 MHz, $CDCl_3$): α anomer**:** δ (selected data) = 65.9 (5c-C), 69.1 (3c-C), 71.3 [*C*H_2Ph (Fuc)], 71.4 (4c-C), 73.2 (5b-C), 75.5 (2c-C), 76.2 (4a-C), 76.6 (4b-C), 77.2 (3b-C), 78.9 (2a-C), 80.1 (3a-C), 80.5 (2b-C), 96.9 (1a-C), 97.2 (1c-C), 102.8 (1b-C); β anomer**:** δ = 65.9 (5c-C), 69.1 (3c-C), 71.3 [*C*H_2Ph (Fuc)], 71.4 (4c-C), 73.2 (5b-C), 74.8 (5a-C), 75.5 (2c-C), 76.1 (4a-C), 76.6 (4b-C), 77.2 (3b-C), 80.5 (s, 2 C, 2b-C, 3b-C), 81.7 (2a-C), 82.8 (3a-C), 97.2 (1c-C), 102.8 (s, 2 C, 1a-C, 1b-C). − MALDI-MS; *m*/*z* = 1270.4 [M + Na^+]. − $C_{75}H_{90}O_{16}$ (1247.54).

8-Hydroxyoctyl 3-*O*-[(3,4,6-Tri-*O*-benzyl-α-D-mannopyranosyl)]-(1→3)-(2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-benzyl-α/β-D-glucopyranoside (2): Trisaccharide **2** was obtained following Procedure B. The residue was purified by flash chromatography (petroleum ether/EtOAc, 6:4→5:5) to afford **2** (66% overall yield from resin **9**) as an oil (α/β = 4:6). − TLC (petroleum ether/EtOAc, 4:6): R_f = 0.41. − ^{1}H NMR (600 MHz, $CDCl_3$): α anomer**:** δ (selected data) = 3.26 (5a-H), 3.28 (5b-H), 3.30 (6b-H), 3.40 (2 H, 2a-H, 6c-H), 3.44 (6′c-H), 3.46 (6′b-H), 3.57 (6a-H), 3.58 (2b-H), 3.63 (6a-H), 3.65 (3b-H), 3.77 (4 H, 2c-H, 3c-H, 4c-H, 3a-H), 3.86 (4a-H), 3.87 (4b-H), 3.99 (5c-H), 4.26 (1b-H), 4.62 (1a-H), 4.96 ($^3J_{1,2}$ < 1 Hz, 1c-H); β anomer**:** δ (selected data) = 3.26 (5a-H), 3.28 (5b-H), 3.30 (6b-H), 3.31 (2a-H), 3.40 (6c-H), 3.44 (6′c-H), 3.46 (2 H, 6′b-H, 3a-H), 3.57 (6a-H), 3.58 (2b-H), 3.63 (6a-H), 3.65 (3b-H), 3.77 (3 H, 2c-H, 3c-H, 4c-H), 3.86 (4a-H), 3.87 (4b-H), 3.99 (5c-H), 4.27 (1a-H), 4.35 (1b-H), 4.95 ($^3J_{1,2}$ < 1 Hz, 1c-H) − ^{13}C NMR (150.9 MHz, $CDCl_3$): α anomer**:** δ (selected data) = 67.7 (6b-C), 68.3 (6a-C, 2c-C), 68.4 (6c-C), 70.6 (5c-C), 72.2 (4b-C), 72.7 (5b-C), 76.3 (3b-C), 76.4 (4a-C), 78.4 (2b-C), 79.2 (2a-C), 80.2 (3a-C), 95.4 (1c-C), 97.0 (1a-C), 102.8 (1b-C); β anomer**:** δ = 67.7 (6b-C), 68.3 (6a-C, 2c-C), 68.4 (6c-C), 70.6 (5c-C), 72.2 (4b-C), 72.7 (5b-C), 75.1 (5a-C), 76.3 (3b-C), 76.4 (4a-C), 78.4 (2b-C), 79.9 (3c-C, 4c-C), 81.8 (2a-C), 82.9 (3a-C), 95.4 (1c-C), 102.7 (1b-C), 103.7 (1a-C). − MALDI-MS; *m*/*z* = 1467.1 [M + Na^+]. − $C_{89}H_{102}O_{17}$ (1443.80).

8-Hydroxyoctyl 3-*O*-[(β-D-Galactopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-dimethylmaleimido-β-D-glucopyranosyl)]-(1→3)-(2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α/β-D-glucopyranoside (3): Compound **3** was obtained following Procedure B. The residue was purified by flash chromatography (EtOAc→EtOAc/MeOH, 96:4) to give **3** (60% overall yield from resin **9**) as an oil (α/β = 4:6). − TLC (EtOAc/MeOH, 96:4): R_f = 0.25. −^{1}H NMR (600 MHz, $CDCl_3$): α anomer**:** δ (selected data) = 3.39 (2a-H), 3.45 (3b-H), 3.63 (5c-H), 3.84 (4a-H), 4.05 (2c-H), 4.09 (4c-H), 4.23 (1b-H), 4.37 (3c-H), 4.45−4.51 (1d-H), 4.62 (1a-H), 5.22 ($^3J_{1,2}$ ≈ 8 Hz, 1c-H); β anomer**:** δ (selected data) = 3.33 (2a-H), 3.45 (3b-H), 3.63 (5c-H), 3.84 (4a-H), 4.05 (2c-H), 4.09 (4c-H), 4.14 (1a-H), 4.32 (1b-H), 4.37 (3c-H), 4.45−4.51 (1d-H), 5.22 ($^3J_{1,2}$ ≈ 8 Hz, 1c-H) − ^{13}C NMR (150.9 MHz, $CDCl_3$): α anomer**:** δ (selected data) = 56.5 (2c-C), 72.9 (5c-C), 76.6 (4a-C), 78.3 (4c-C), 78.4 (3c-C), 79.5 (2a-C), 82.3 (3b-C), 97.3 (1a-C), 100.3 (1c-C), 103.1 (1d-C), 103.8 (1b-C); β anomer**:** δ = 56.5 (2c-C), 72.9 (5c-C), 76.6 (4a-C), 78.3 (4c-C), 78.4 (3c-C), 82.2 (2a-C), 82.3 (3b-C), 100.3 (1c-C), 102.8 (2 C, 1a-C, 1b-C), 103.1 (1d-C). − MALDI-MS; *m*/*z* = 1646.1 [M + Na^+]. − $C_{94}H_{111}NO_{23}$ (1622.93).

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[1] M. L. Osborn, H. K. Tariq, *Tetrahedron* **1999**, *55*, 1807−1850.
[2] W. C. Haase, P. H. Seeberger, *Curr. Org. Chem.* **2000**, *4*, 481−511.
[3] For some applications on Merrifield resin, see: [3a] L. Knerr, R. R. Schmidt, *Eur. J. Org. Chem.* **2000**, 2803−2808. − [3b] L. Knerr, R. R. Schmidt, *Synlett* **1999**, 1802−1804. − [3c] J. Rademann, A. Geyer, R. R. Schmidt, *Angew. Chem.* **1998**, *110*, 1309−1313; *Angew. Chem. Int. Ed.* **1998**, *37*, 1241−1245. − [3d] J. Rademann, R. R. Schmidt, *J. Org. Chem.* **1997**, *62*, 3650−3656. − [3e] J. Rademann, R. R. Schmidt, *Tetrahedron Lett.* **1996**, *37*, 3989−3990. − [3f] For one application on CPG, see: A. Heckel, E. Mross, K. H. Jung, J. Rademann, R. R. Schmidt, *Synlett* **1998**, 171−173.
[4] H. Shimizu, Y. Ito, O. Kanie, T. Ogawa, *Bioorg. Med. Chem. Lett.* **1996**, *6*, 2841−2846.
[5] For an application on a PEG solid phase: Z. H. Wang, S. P. Douglas, J. I. Krepinsky, *Tetrahedron Lett.* **1996**, *37*, 6985−6988 and references cited therein.
[6] R. R. Schmidt, *Angew. Chem.* **1986**, *98*, 213−236; *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 212−235.
[7] W. Kinzy, R. R. Schmidt, *Adv. Carbohydr. Chem. Biochem.* **1994**, *50*, 21−123.
[8] F. Roussel, L. Knerr, M. Grathwohl, R. R. Schmidt, *Org. Lett.* **2000**, *2*, 3043−3046.
[9] S. J. Freese, W. F. Vann, *Carbohydr. Res.* **1996**, *281*, 313−319.
[10] For Fmoc-containing thioglycoside donors, see: [10a] K. C. Nicolaou, N. Winssinger, J. Pastor, F. DeRoose, *J. Am. Chem. Soc.* **1997**, *119*, 449−450. − [10b] K. C. Nicolaou, N. Watanabe, J. Li, J. Pastor, N. Winssinger, *Angew. Chem. Int. Ed.* **1998**, *37*, 1559−1561. − [10c] T. Zhu, G.-J. Boons, *Tetrahedron: Asymmetry* **2000**, *11*, 199−205.
[11] For other uses of ester-type linkers on solid-phase, see: [11a] Ref.[4] − [11b] S. Manabe, Y. Ito, T. Ogawa, *Synlett* **1998**, 628−630.
[12] The successful synthesis of **1** was already reported in a short communication; see ref.[8]
[13] K.-H. Jung, M. Hoch, R. R. Schmidt, *Liebigs Ann. Chem.* **1989**, 1099−1106.
[14] J. Alais, A. Maranduba, A. Veyrières, *Tetrahedron Lett.* **1983**, *24*, 2383−2386.
[15] B. M. Trost, C. G. Caldwell, E. Murayama, D. Heissler, *J. Org. Chem.* **1983**, *48*, 3252−3265.
[16] R. Windmüller, Diplomarbeit, Universität Konstanz, Germany, **1991**.
[17] R. Windmüller, R. R. Schmidt, *Tetrahedron Lett.* **1994**, *35*, 7927−7930.
[18] For use in solution see: [18a] S. P. Douglas, D. M. Whitfield, J. J. Keprinsky, *J. Am. Chem. Soc.* **1991**, *113*, 5095−5097. − [18b] T. G. Mayer, B. Kratzer, R. R. Schmidt, *Angew. Chem.* **1994**, *106*, 2289−2293; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2177−2181.
[19] For use on solid phase; see ref.[3d]
[20] M. R. E. Aly, J. C. Castro-Palomino, E.-S. I. Ibrahim, E.-S. H. El-Ashry, R. R. Schmidt, *Eur. J. Org. Chem.* **1998**, 2305−2316.
[21] M. R. E. Aly, E.-S. I. Ibrahim, E.-S. H. El-Ashry, R. R. Schmidt, *Carbohydr. Res.* **1999**, *316*, 121−132.

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