Synthesis of Lacto-*N*-neohexaose and Lacto-*N*-neooctaose Using the Dimethylmaleoyl Moiety as an Amino Protective Group

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Keywords: Carbohydrates / Amino sugars / Protecting groups / Glycosylations / Trichloroacetimidates / Oligosaccharides

The *N*-DMM-Protected lactosamine derivative **2** was readily transformed into the corresponding glycosyl donor **4** and into acceptor **5**. A TMSOTf-catalyzed glycosidation afforded the derived tetrasaccharide **6** which led to glycosyl donor **9**. Reaction of **9** with lactose derivative **10** as acceptor gave the desired hexasaccharide **11**. Cleavage of all protective groups and *N*-acetylation afforded the target molecule **1b** (lacto-*N*-neohexaose). Glycosylation of acceptor **10** with donor **4** furnished tetrasaccharide **16** which, employing standard procedures, gave acceptor **18**. Glycosylation of **18** with donor **9** furnished, under standard conditions, octasaccharide **19**. Cleavage of all protective groups and *N*-acetylation afforded the target molecule **1c** (lacto-*N*-neooctaose). Both **1b** and **1c** were obtained in good overall yields.

Introduction

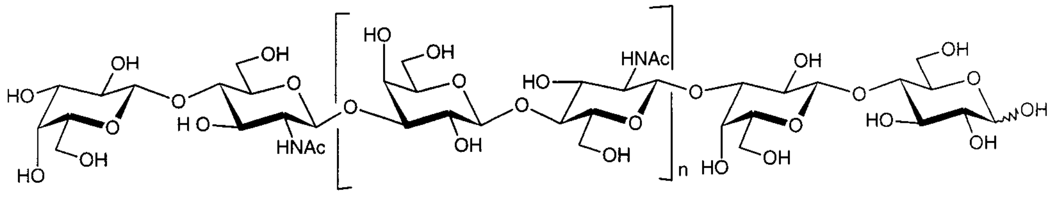
A β(1−3)-linked *N*-acetyllactosamine chain, which is connected via a β(1−3)-linkage to lactose (Scheme 1. **1a**: lacto-*N*-neotetraose; **1b**: lacto-*N*-neohexaose; **1c**: lacto-*N*-neooctaose), is a frequently occurring structural unit. For instance, this type of compounds is found in human milk.[1][2] Various biological functions are connected with this structural unit.[3][4] Therefore, its chemical synthesis has already been investigated in solution,[5] as well as in the solid phase.[6] One of the crucial points in the synthesis of oligosaccharides requiring 2-amino-2-deoxy-D-glucose (glucosamine) is the availability of versatile donor and acceptor building blocks that possess suitable protection of the amino group.

Various protecting groups for such purposes are available.[7][8] Recently, we introduced the dimethylmaleoyl (DMM) group as a new protective group for glucosamine.[9] Its ease of attachment and subsequent cleavage, and its electron-withdrawing property, make the glucosamine derivative a good glycosyl donor with an enhanced capability to form β-linkages. Moreover, versatile glycosyl acceptors containing the dimethylmaleoylamido group could also be generated and successfully employed in glycosylation reactions.[4][9] Owing to these properties of the DMM group, we report herein its highly successful application to the synthesis of lacto-*N*-neohexaose (**1b**) and lacto-*N*-neooctaose (**1c**), thus demonstrating its competitiveness with previously reported procedures for lacto-*N*-neo"oligo"ose synthesis.

Results and Discussion

N-DMM-Protected Lactosamine for the Synthesis of 1b

As recently reported, the *N*-DMM-protected lactosamine derivative **2** (Scheme 2) is readily available from *O*-(tetra-*O*-acetyl-α-D-galactopyranosyl) trichloroacetimidate as donor and *tert*-butyldimethylsilyl 3,6-di-*O*-benzyl-2-deoxy-2-maleimido-β-D-glucopyranoside as acceptor, in high yield.[4] Compound **2** can be transformed into trichloroacetimidate **4**, a glycosyl donor, in high overall yield by 1-*O*-desilylation with tetrabutylammonium fluoride (TBAF) in acetic acid and subsequent reaction with trichloroacetonitrile in the presence of 1,8-diaza-[5.4.0] bicycloundec-7-ene (DBU) as base.



1a: n = 0; **1b**: n = 1; **1c**: n = 2

Scheme 1. Structure of lacto-*N*-neooligosaccharides

Treatment of **2** with sodium methanolate in methanol (Zemplén conditions[10]) led to deacylation (→ **3**) and reaction with benzaldehyde dimethylacetal in the presence of *para*-toluenesulfonic acid (*p*-TsOH) as catalyst furnished

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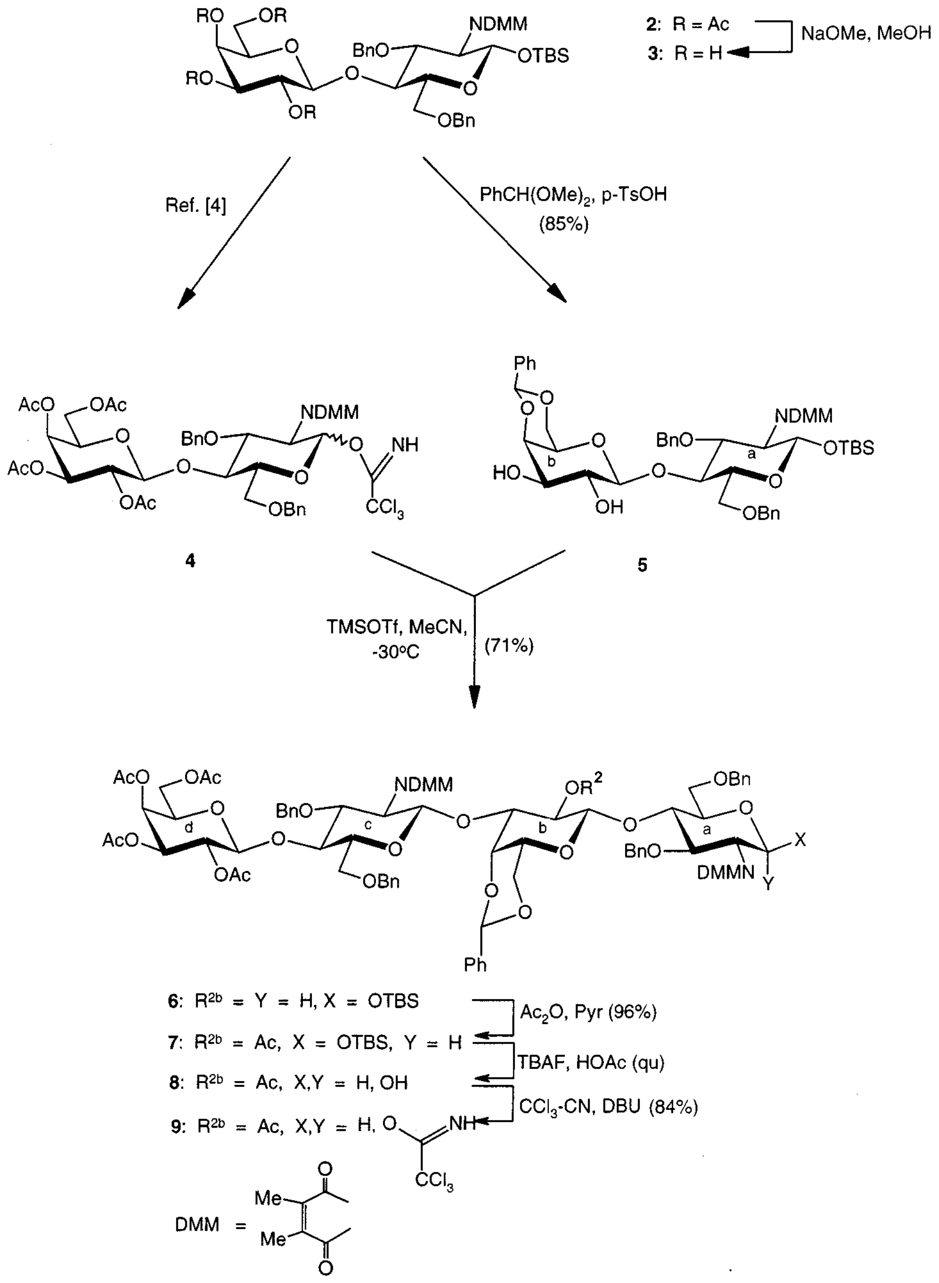


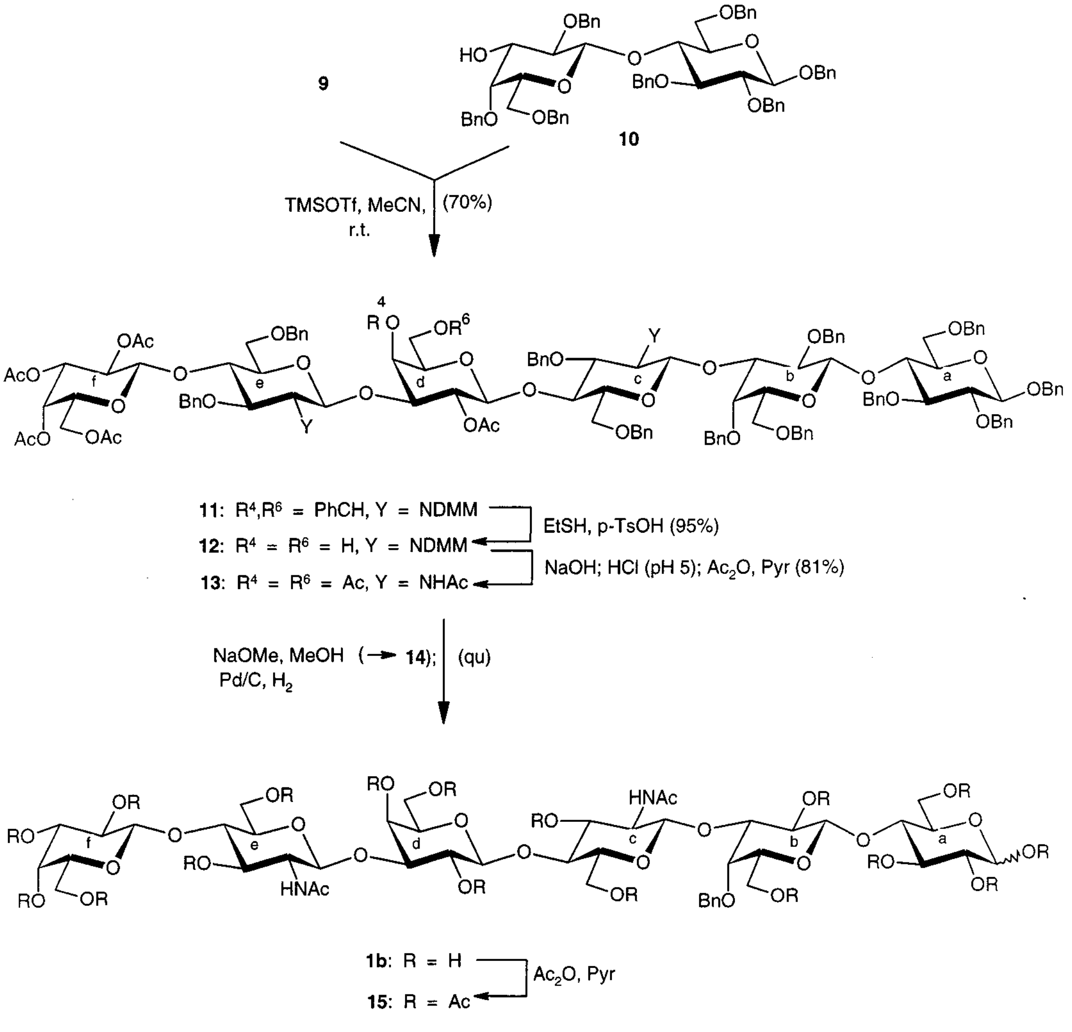
Scheme 2. Synthesis of tetrasaccharide intermediate **9**

the 4b,6b-*O*-benzylidene derivative **5**. Glycosylation with **4**[4] as donor and **5** as acceptor in the presence of trimethylsilyl trifluoromethanesulfonate (TMSOTf) as catalyst in acetonitrile as solvent (use of the "nitrile effect",[11] i.e., the use of *N*-glycosylnitrilium intermediates as glycosylating agents) at −40°C gave regioselectively the β(1−3)-linkage, thus affording the desired tetrasaccharide **6** which contains two lactosamine residues. Reaction of **6** with acetic anhydride in pyridine led to a 2b-*O*-acetylation giving compound **7**. The β(1−3)-linkage of the two lactosamine residues could be derived from the NMR spectroscopic data of **6** and **7** [^{1}H NMR: **6:** δ = 3.45 (3b-H), 3.63−3.74 (2b-H), 5.31 ($J_{1,2}$ = 7.3 Hz, 1c-H); **7:** δ = 3.69−3.73 (3b-H), 5.10−5.14 (2b-H), 5.09 ($J_{1,2}$ = 8.4 Hz, 1c-H)]. Subsequent treatment of **7** with TBAF in acetic acid led to quantitative desilylation (→ **8**) and then reaction with trichloroacetonitrile in the presence of DBU as base afforded trichloroacetimidate **9**.

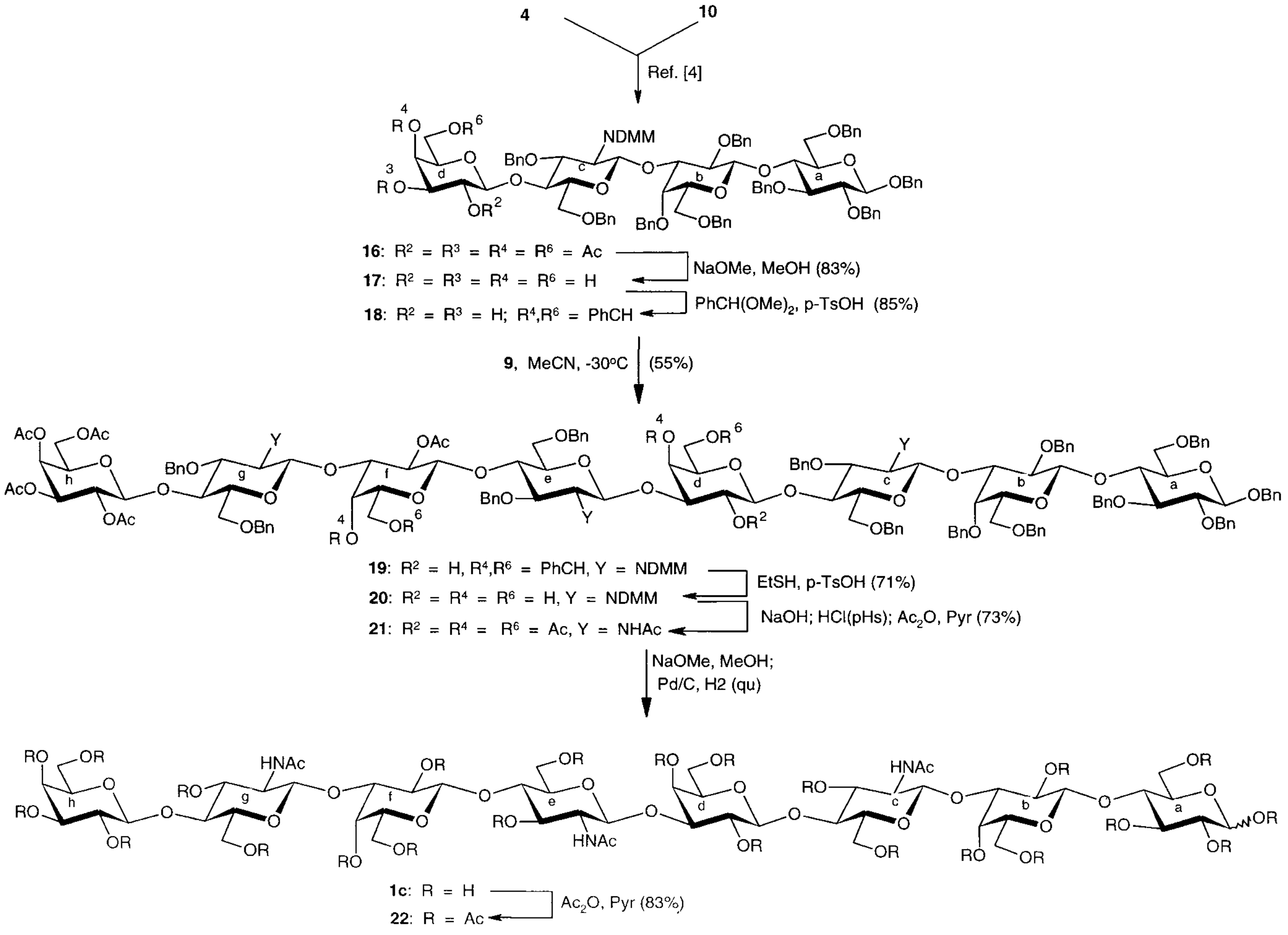
Glycosylation of the known 3b-*O*-unprotected lactose derivative **10**[12][13] (Scheme 3) as acceptor with **9** as donor, in the presence of TMSOTf as catalyst, in acetonitrile at room temperature afforded the desired hexasaccharide **11** in 70% yield (^{1}H NMR: 1c-H: $J_{1,2}$ = 8.3 Hz). The 4d,6d-*O*-benzylidene group was then cleaved with ethylmercaptan as nucleophile and *p*-TsOH as catalyst[14,15] affording compound **12** in high yield. The two DMM groups were removed by treatment with sodium hydroxide and then with hydrochloric acid at pH = 5.[9] Acetylation with acetic anhydride in pyridine gave the desired *N*-acetylated compound **13** in 81% yield. Treatment of **13** with sodium methanolate in methanol led to complete de-*O*-acetylation (→ **14**); subsequent hydrogenolytic *O*-debenzylation with palladium on carbon as catalyst in a 1:1:1-mixture of methanol/acetic acid/dioxane gave the desired lacto-*N*-neohexaose **1b**. For complete structural assignment, **1b** was acetylated with acetic anhydride in pyridine to afford the per-*O*-acetyl derivative **15** which showed the expected NMR spectrum [^{1}H NMR: 4.32, 4.33 (2 d, $J_{1,2}$ = 9.7 Hz, 1 H, $1b_\alpha$- and $1b_\beta$-H), 4.40 (d, $J_{1,2}$ = 7.7 Hz, 1 H, 1d-H), 4.53 (d, $J_{1,2}$ = 7.9 Hz, 1 H, 1f-H), 4.63 (2 d, $J_{1,2}$ = 7.7, 8.0 Hz, 1 H, $1c_\beta$- and $1c_\alpha$-H), 4.69 (d, $J_{1,2}$ = 7.5 Hz, 1 H, 1e-H), 5.65 (d, $J_{1,2}$ = 8.2 Hz, 0.56 H, $1a_\beta$-H), 6.24 (d, $J_{1,2}$ = 3.5 Hz, 0.44 H, $1a_\alpha$-H)].

Synthesis of Lacto-*N*-neooctaose (1c)

With the available building blocks the synthesis of target molecule **1c** could be readily accomplished. Thus, reaction of glycosyl donor **4** with acceptor **10**[12][13] afforded the tetrasaccharide **16** (Scheme 4) as previously described.[4] Removal of all *O*-acetyl groups by treatment with sodium methanolate in methanol furnished the 2d,3d,4d,6d-*O*-unprotected derivative **17**. Reaction of **17** with benzaldehyde dimethylacetal in the presence of *p*-TsOH as catalyst afforded the 2d,3d-*O*-unprotected tetrasaccharide **18**. As expected, **18** exhibited the same glycosyl acceptor properties as **5**; thus, reaction with the tetrasaccharide donor **9** in the presence of TMSOTf as catalyst in acetonitrile at −30°C afforded the octasaccharide **19** in good yield. Removal of the protective groups was performed as described above: cleavage of two benzylidene groups (→ **20**), then cleavage of three DMM groups and ensuing *N*-acetylation (→ **21** in 73% yield), and complete de-*O*-acetylation and hydrogenolytic debenzylation gave lacto-*N*-neooctaose **1c** in quantitative yield. For the structural assignment, **1c** was transformed into the per-*O*-acetyl derivative **22** (2:3 α/β-mixture) which exhibited the expected NMR spectrum [^{1}H NMR: 4.34 (d, $J_{1,2}$ = 8.0 Hz, 1 H, 1b-H), 4.42 (d, $J_{1,2}$ = 9.7 Hz, 2 H, 1d-H, 1f-H), 4.55 (d, $J_{1,2}$ = 9.7 Hz, 1 H, 1h-H), 4.64, 4.67, 4.69 (3 d, $J_{1,2}$ = 9.7 Hz, 3 H, 1c-H, 1e-H, 1g-H), 5.66 (d, $J_{1,2}$ = 8.2 Hz, 0.6 H, $1a_\beta$-H), 6.25 (d, $J_{1,2}$ = 3.5 Hz, 0.4 H, $1a_\alpha$-H)].



Scheme 3. Synthesis of lacto-*N*-neohexaose **1b**



Scheme 4. Synthesis of lacto-*N*-neooctaose **1c**

In conclusion, DMM-protected lactosamine could be transformed into glycosyl donors and acceptors. Glycosylation reactions with the DMM-protected lactosamine donors furnished only β-glycosides. The DMM group is compatible with various manipulations of other protective groups. Cleavage of up to three DMM groups in a one-pot reaction under standard conditions worked reliably and in good yields. Hence, the DMM group is a very useful amino protective group in oligosaccharide synthesis.

Experimental Section

Solvents were purified in the usual way. − Melting points are uncorrected. − TLC was performed on plastic plates Silica Gel 60 F_{254} and on HPTLC plates NH_2 F_{254} S (E Merck, layer thickness 0.2 mm). − Detection was achieved by treatment with a solution 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 150°C. Flash chromatography was carried out on silica gel (Baker, 30−60 μm) and Lichroprep NH_2, particle size 40−63 μm. − Medium pressure liquid chromatography (MPLC): LiChroprep Si 60 (Merck; Korngröße 15−25 μm), detection by differential refractometer. 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. The assignment of ^{1}H NMR spectra were based on chemical shift correlation (DQFCOSY) and Rotating Frame Nuclear Overhauser Effect Spectroscopy (ROESY). − The assignment of ^{13}C NMR spectra was based on Carbon-Proton Shift-Correlation Heteronuclear Multiple Quantum Coherence (HMQC). − MS spectra were recorded with MALDI-Kompakt (Kratos) and FAB with Finningen MAT 312/AMD. Microanalyses were performed in the unit of Microanalysis at the Fakultät für Chemie, Universität Konstanz.

***tert*-Butyldimethylsilyl *O*-(-β-D-Galactopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-dimethylmaleimido-β-D-glucopyranoside (3):** A solution of **2**[4] (308 mg, 0.337 mmol) in dry methanol (3.18 mL) was stirred at room temp. while NaOMe (0.195 M, 0.17 mL) was added dropwise. After 90 min the solution was neutralized by Amberlite IR resin (H^+form), filtered and dried in vacuo. The residue was purified by flash chromatography (toluene/acetone, 1:1) to yield **3** (228 mg, 83%) as an amorphous mass. − TLC (toluene/acetone, 1:1): R_f = 0.14; $[\alpha]_D$ = + 43.0 (*c* = 0.46, chloroform). − ^{1}H NMR (250 MHz, $CDCl_3$ + 10 μL D_2O): δ = −0.08 (s, 3 H, $SiCH_3$), 0.02 (s, 3 H, $SiCH_3$), 0.74 [s, 9 H, $SiC(CH_3)_3$], 1.78 (br.s, 6 H, 2 CH_3), 3.27−3.96 (m, 10 H, 5b-H, 3b-H, 2b-H, 5a-H, 6b-H, 6′b-H, 6a-H, 2a-H, 4b-H, 6′a-H), 4.03 (dd, $J_{3,4}$ = $J_{4,5}$ = 8.8 Hz, 1 H, 4a-H), 4.27 (dd, $J_{2,3}$ = 10.7, $J_{3,4}$ = 8.8 Hz, 1 H, 3a-H), 4.44, 4.86 (2 d, J_{gem} = 12.4 Hz, 2 H, CH_2Ph), 4.55 (d, $J_{1,2}$ = 7.6 Hz, 1 H, 1b-H), 4.58, 4.71 (2 d, J_{gem} = 12.3 Hz, 2 H, CH_2Ph), 5.11 (d, $J_{1,2}$ = 8.1 Hz, 1 H, 1a-H), 7.13−7.34 (m, 10 H, 2 Ph). − MALDI-

MS (positive mode, DHB/THF matrix) *m*/*z*: 766 [MNa$^+$]. − $C_{38}H_{53}NO_{12}Si$ (743.89): calcd. C 61.35, H 7.18, N 1.88; found C 61.63, H 7.72, N 1.24.

***tert*-Butyldimethylsilyl *O*-(4,6-*O*-Benzylidene-β-D-galactopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-dimethylmaleimido-β-D-glucopyranoside (5):** A mixture of **3** (757 mg, 1.017 mmol), benzaldehyde dimethylacetal (202 mg, 1.332 mmol, 0.2 mL) and *p*-TsOH (0.016 g, 0.084 mmol) in dry acetonitrile (5 mL) was stirred at room temp. After 20 h the solution was neutralized with triethylamine and evaporated in vacuo. The residue was purified by flash chromatography (petroleum ether/ethyl acetate, 1:1) to yield **5** (723 mg, 85%) as a white foam. − TLC (petroleum ether/ethyl acetate, 1:1): R_f = 0.13; $[\alpha]_D$ = +38.0 (*c* = 0.2, chloroform). − ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.02 (s, 3 H, $SiCH_3$), 0.13 (s, 3 H, $SiCH_3$), 0.83 [s, 9 H, $SiC(CH_3)_3$], 1.90 (br.s, 6 H, 2 CH_3), 2.51 (s, 1 H, 3b-OH), 2.52 (s, 1 H, 2b-OH), 3.19 (br.s, 1 H, 5b-H), 3.62 (dd, $J_{2,3}$ = 9.0, $J_{3,4}$ = 3.8 Hz, 1 H, 3b-H), 3.66−3.70 (m, 1 H, 5a-H), 3.78 (dd, $J_{1,2}$ = 7.6, $J_{2,3}$ = 9.0 Hz, 1 H, 2b-H), 3.84 (dd, J_{gem} = 11.6, $J_{5,6}$ = 1.9 Hz, 1 H, 6a-H), 3.96 (dd, J_{gem} = 12.4, $J_{5,6}$ = 1.7 Hz, 1 H, 6b-H), 4.00 (dd, $J_{1,2}$ = 8.1, $J_{2,3}$ = 10.9 Hz, 1 H, 2a-H), 4.12 (dd, J_{gem} = 11.6, $J_{5,6'}$ = 3.1 Hz, 1 H, 6′a-H), 4.16−4.19 (m, 2 H, 4a-H, 4b-H), 4.25 (dd, J_{gem} = 12.4, $J_{5,6'}$ < 1.0 Hz, 1 H, 6′b-H), 4.41 (dd, $J_{2,3}$ = 10.9, $J_{3,4}$ = 8.8 Hz, 1 H, 3a-H), 4.63, 5.05 (2 d, J_{gem} = 12.4 Hz, 2 H, C*H*2Ph), 4.69 (d, $J_{1,2}$ = 7.6 Hz, 1 H, 1b-H), 4.71, 4.82 (2 d, J_{gem} = 12.3 Hz, 2 H, C*H*2Ph), 5.22 (d, $J_{1,2}$ = 8.1 Hz, 1 H, 1a-H), 5.56 (s, 1 H, C*H*Ph), 7.26−7.53 (m, 15 H, 3 Ph). − ^{13}C NMR (150.9 MHz, $CDCl_3$): δ = −5.56 ($SiCH_3$), −4.20 ($SiCH_3$), 8.00 (2 CH_3−C), 25.34 [$SiC(CH_3)_3$], 58.20 (2a-C), 66.90 (5b-C), 68.70 (6a-C), 69.30 (6b-C), 73.00 (2b-C), 73.10 (3b-C), 73.80 (*C*H_2Ph), 74.90 (5a-C, *C*H_2Ph), 79.10 (4a-C), 79.20 (3a-C), 93.90 (1a-C), 101.70 (*C*HPh), 103.80 (1b-C), 126.42−139.16 (3 Ph-C). − MALDI-MS (positive mode, DHB/THF matrix) *m*/*z*: 854.8 [MNa$^+$], 871 [MK$^+$]. − $C_{45}H_{57}NO_{12}Si$ (832.00): calcd. C 64.95, H 6.90, N 1.68; found C 65.13, H 7.02, N 1.44.

***tert*-Butyldimethylsilyl *O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-(3,6-di-*O*-benzyl-2-deoxy-2-dimethylmaleimido-β-D-glucopyranosyl)-(1→3)-(4,6-*O*-benzylidene-β-D-galactopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-dimethylmaleimido-β-D-glucopyranosid (6):** A mixture of **4**[4] (95 mg, 1.008 mmol) and **5** (77 mg, 0.925 mmol) in dry acetonitrile (4 mL) was stirred under nitrogen at −25 °C while TMSOTf (0.01 M in acetonitrile, 1.05 mL) was added dropwise. After 45 min the reaction mixture was neutralized with Et_3N and dried in vacuo. The residue was purified by flash chromatography (petroleum ether/ethyl acetate, 1.5:1) to yield **6** (1068 mg, 71%) as a white foam. − TLC (petroleum ether/ethyl acetate, 1.5:1): R_f = 0.12; $[\alpha]_D$ = +2.5 (*c* = 0.4, chloroform). − ^{1}H NMR (600 MHz, $CDCl_3$): δ = −0.10 (s, 3 H, $SiCH_3$), −0.02 (s, 3 H, $SiCH_3$), 0.71 [s, 9 H, $SiC(CH_3)_3$], 1.71, 1.76, 1.95, 1.98, 2.06 (5 s, 24 H, 4 CH_3, 4 CH_3CO), 2.98−3.00 (br.s, 2 H, OH, 5b-H), 3.45 (dd, $J_{2,3}$ = 9.8, $J_{3,4}$ = 3.5 Hz, 1 H, 3b-H), 3.50−3.51 (m, 2 H, 5a-H, 5c-H), 3.63−3.74 (m, 6 H, 5d-H, 2b-H, 6d-H, 6b-H, 6c-H, 6`c-H), 3.84 (dd, $J_{1,2}$ = 8.1, $J_{2,3}$ = 10.9 Hz, 1 H, 2a-H), 3.92−3.98 (m, 6 H, 6a-H, 6′a-H, 6′d-H, 4c-H, 2c-H, 4a-H), 4.03 (d, $J_{3,4}$ = 2.7 Hz, 1 H, 4b-H), 4.07−4.09 (m, 2 H, 6′b-H, 3c-H), 4.21 (dd, $J_{2,3}$ = 10.7, $J_{3,4}$ = 8.7 Hz, 1 H, 3a-H), 4.36, 4.80 (2 d, J_{gem} = 12.4 Hz, 2 H, C*H*2Ph),4.43, 4.71 (2 d, J_{gem} = 11.9 Hz, 2 H, C*H*2Ph), 4.45, 4.80 (2 d, J_{gem} = 12.3 Hz, 2 H, C*H*2Ph), 4.47 (d, $J_{1,2}$ = 7.6 Hz, 1 H, 1b-H), 4.53, 4.63 (2 d, J_{gem} = 12.3 Hz, 2 H, C*H*2Ph), 4.56 (d, $J_{1,2}$ = 8.0 Hz, 1 H, 1d-H), 4.84 (dd, 1 H, $J_{2,3}$ = 10.4, $J_{3,4}$ = 3.3 Hz, 1 H, 3d-H), 5.07 (d, $J_{1,2}$ = 8.1 Hz, 1 H, 1a-H), 5.12 (dd, $J_{1,2}$ = 8.0, $J_{2,3}$ = 10.4, 1 H, 2d-H), 5.25 (d, $J_{3,4}$ = 3.3 Hz, 1 H, 4d-H), 5.31 (d, $J_{1,2}$ 0 7.3 Hz, 1 H, 1c-H), 5.32 (s, 1 H, C*H*Ph), 7.11−7.34 (m, 25 H, 5 Ph). − ^{13}C NMR (150.9 MHz, $CDCl_3$): δ = 55.20 (2c-C), 57.60 (2a-C), 60.60 (6a-C),66.30 (5b-C), 66.80 (4d-C), 67.90 (6c-C), 68.10 (6d-C), 68.70 (6b-C), 69.40 (2d-C), 70.30 (5d-C), 70.50 (2b-C), 70.80 (3d-C), 73.30 (*C*H_2Ph), 73.70 (*C*H_2Ph), 74.00 (*C*H_2Ph), 74.50 (*C*H_2Ph), 74.60 (5a-C, 5c-C), 75.20 (4b-C), 77.30 (3c-C), 78.00 (4c-C), 78.30 (3a-C), 78.40 (4a-C), 79.10 (3b-C), 93.40 (1a-C),99.00 (1c-C), 100.30 (1d-C), 100.40 (*C*HPh), 103.10 (1b-C). − MALDI-MS (positive mode, DHB/THF matrix) *m*/*z*: 1633.4 [MNa$^+$]. − $C_{85}H_{102}N_2O_{27}Si$ (1611.77): calcd. C 63.77, H 6.37, N 1.73; found C 63.34, H 6.46, N 1.34.

***tert*-Butyldimethylsilyl *O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-(3,6-di-*O*-benzyl-2-deoxy-2-dimethylmaleimido-β-D-glucopyranosyl)-(1→3)-(2-*O*-acetyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-dimethylmaleimido-β-D-glucopyranoside (7):** A mixture of **6** (1068 mg, 0.662 mmol), pyridine (16 mL) and acetic anhydride (8 mL) was stirred overnight and then coevaporated with toluene in vacuo. The residue was dissolved in dichloromethane (30 mL) and washed successively with HCl (3%, 30 mL), water (20 mL) and saturated $NaHCO_3$ (30 mL), and then dried over $MgSO_4$ and evaporated in vacuo. The residue was purified by flash chromatography (petroleum ether/ethyl acetate, 1.5:1) to yield **7** (1058 mg, 96%) as an amorphous mass. − TLC (petroleum ether/ethyl acetate, 1.5:1): R_f = 0.12; $[\alpha]_D$ = +3.2 (*c* = 1.2, chloroform). − ^{1}H NMR (600 MHz, $CDCl_3$): δ = −0.05 (s, 3 H, $SiCH_3$), 0.05 (s, 3 H, $SiCH_3$), 0.76 [s, 9 H, $SiC(CH_3)_3$], 1.66, 1.74, 1.86, 1.96, 2.01, 2.03, 2.06, 2.12 (8 s, 27 H, 4 CH_3, 5 CH_3CO), 3.19 (br.s, 1 H, 5b-H), 3.43 (m, 1 H, 5a-H), 3.58 (m, 1 H, 5c-H), 3.69−3.73 (m, 3 H, 5d-H, 3b-H, 6a-H), 3.76 (dd, $J_{5,6}$ = 3.5, 1 H, 6′a-H), 3.81 (br.s, 2 H, 6c-H, 6′c-H), 3.84−3.87 (m, 2 H, 2a-H, 6b-H), 3.91 (dd, $J_{3,4}$ = $J_{4,5}$ = 9.6 Hz, 1 H, 4a-H), 3.95−4.00 (m, 4 H, 6d-H, 6′d-H, 2c-H, 4c-H), 4.09 (dd, $J_{2,3}$ = 10.7, $J_{3,4}$ = 8.6 Hz, 1 H, 3a-H), 4.16−4.17 (m, 2 H, 3c-H, 4b-H), 4.25 (d, J_{gem} = 12.2 Hz, 1 H, 6`b-H), 4.39, 4.99 (2 d, J_{gem} = 12.6 Hz, 2 H, C*H*$_2$Ph), 4.41, 4.85 (2d, J_{gem} = 12.3 Hz, 2 H, C*H*$_2$Ph), 4.45 (d, $J_{1,2}$ = 7.9 Hz, 1 H, 1b-H), 4.54, 4.78 (2 d, J_{gem} = 12.0 Hz, 4 H, 2 C*H*$_2$Ph), 4.62 (d, J_{gem} = 8.0 Hz, 1 H, 1d-H), 4.90 (dd, $J_{2,3}$ = 10.4, $J_{3,4}$ = 3.5 Hz, 1 H, 3d-H), 5.09 (d, $J_{1,2}$ = 8.4 Hz, 1 H, 1c-H), 5.10−5.14 (m, 2 H, 1a-H, 2b-H), 5.18 (dd, $J_{1,2}$ = 8.0, $J_{2,3}$ = 10.4 Hz, 1 H, 2d-H), 5.30 (d, $J_{3,4}$ = 3.5 Hz, 1 H, 4d-H), 5.45 (s, 1 H, C*H*Ph), 7.13−7.41 (m, 25 H, 5 Ph). − ^{13}C NMR (150.9 MHz, $CDCl_3$): δ = −5.64 ($SiCH_3$), −4.28 ($SiCH_3$), 8.57 (4 CH_3), 17.53 [$SiC(CH_3)_3$], 20.50, 20.55, 20.59, 20.74, 21.05 (5 CH_3CO), 25.29 [$SiC(CH_3)_3$], 55.17 (2c-C), 57.60 (2a-C), 60.79 (6d-C), 66.40 (5b-C), 66.90 (4d-C), 67.95 (6c-C, 6a-C), 68.40 (6b-C), 69.55 (2d-C), 70.50 (5d-C), 70.92 (3d-C), 74.23 (*C*H_2Ph), 74.64 (5c-C, 2 *C*H_2Ph), 74.98 (*C*H_2Ph), 75.24 (5a-C), 75.65 (3b-C), 75.72 (4b-C), 77.17 (3c-C), 77.43 (3a-C), 78.14 (4c-C), 78.29 (4a-C), 93.27 (1a-C), 98.67 (1c-C), 100.28 (*C*HPh−C), 100.43 (1d-C), 100.72 (1b-C), 126.12−139.29 (5 Ph-C), 168.90, 169.14, 169.97, 170.12, 170.25 (C=O). − MALDI-MS (positive mode, DHB/THF matrix) *m*/*z*: 1677.8 [MNa$^+$], 1694.1 [MK$^+$]. − $C_{87}H_{104}N_2O_{28}Si$ (1653.80): calcd. C 63.17, H 6.33, N 1.69; found C 63.29, H 6.56, N 1.36.

***O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-(3,6-di-*O*-benzyl-2-deoxy-2-dimethylmaleimido-β-D-glucopyranosyl)-(1→3)-(2-*O*-acetyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)-(1→4)-(3,6-di-*O*-benzyl-2-deoxy-2-dimethylmaleimido-α/β-D-glucopyranosyl) trichloroacetimidate (9):** A mixture of **7** (1056 mg, 0.638 mmol) and glacial acetic acid (42 mg, 0.699 mmol, 0.04 mL) in dry THF (3 mL) was stirred under nitrogen in an ice-salt bath while TBAF (0.65 mL, 0.65 mmol) was added dropwise. After 30 min the bath was removed and the mixture stirred at room temp. overnight. The reaction mixture was diluted with a saturated NaCl solution and then extracted with dichloromethane (3 × 20 mL). The organic layers were collected, dried over $MgSO_4$ and evaporated in vacuo. The residue was purified by flash chromatography (ethyl acetate/petroleum ether, 2:1) to yield **8** (98 mg, 100%) as a white foam. − TLC (ethyl acetate/petroleum ether, 2:1): R_f = 0.25, 0.34 for the α,β anomers. − A mixture of this foam (98 mg, 0.638 mmol), trichloroacetonitrile (144 mg, 9.97 mmol, 1.0 mL) and DBU (50 mg, 0.334 mmol, 0.05 mL) in dry dichloromethane (3 mL) was stirred at room temp. After 9 h the reaction mixture was concentrated in vacuo and purified by flash chromatography (petroleum ether/ethyl acetate, 1:1 + 1% Et_3N) to yield **9** (0.922 g, 84%) as a yellow foam in the ratio α,β ≈ 1:1. − TLC (petroleum ether/ethyl acetate, 1:1, + 1% Et_3N): R_f = 0.44. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.74−2.09 (several s, 27 H, 4 CH_3, 5 CH_3CO), 3.12−5.19 (m, 34 H), 5.27 (d, $J_{3,4}$ = 3.3 Hz, 1 H, 4d-H), 5.42 (s, 1 H, C*H*Ph), 6.16 (d, $J_{1,2}$ = 7.8 Hz, 0.5 H, 1a$_\beta$-H), 6.17 (d, $J_{1,2}$ = 4.1 Hz, 0.5 H, 1a$_\alpha$-H), 7.06−7.37 (m, 25 H, 5 Ph), 8.53 (s, 1 H, NH). − FAB-MS (positive mode, NBOH/NaI matrix) *m*/*z*: 1707 [MNa$^+$], 1856 [MNaI]Na$^+$. − $C_{83}H_{90}N_3O_{28}Cl_3$ (1683.94): calcd. C 59.19, H 5.38, N 2.49; found C 58.73, H 5.77, N 2.28.

Benzyl *O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-(3,6-di-*O*-benzyl-2-deoxy-2-dimethylmaleimido-β-D-glucopyranosyl)-(1→3)-(2-*O*-acetyl-4,6-*O*-benzylidene-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-β-D-glucopyranoside (11): A mixture of **9** (303 mg, 0.179 mmol) and **10**[12][13] (139 mg, 0.142 mmol) in dry acetonitrile (1.5 mL) was stirred at room temp. under nitrogen while TMSOTf (0.01 M in acetonitrile, 0.19 mL) was added dropwise. After 45 min the reaction mixture was neutralized by Et_3N and evaporated in vacuo. The residue was purified by flash chromatography (petroleum ether/ethyl acetate, 1.25:1) to yield 11 (250 mg, 70%) as a white foam. − TLC (petroleum ether/ethyl acetate, 1.25:1): R_f = 0.17; $[\alpha]_D$ = −19.2 (*c* = 0.13, chloroform). − ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.24, 1.59, 1.78 (3 br.s, 12 H, 4 CH_3), 1.92, 1.97, 1.99, 2.02, 2.08 (5 s, 15 H, 5 CH_3CO), 3.00 (m, 1 H, 5a-H), 3.11 (br.s, 1 H, 5d-H), 3.33−3.65 (m, 11 H, 6b-H, 5b-H, 6a-H, 2a-H, 3a-H, 5c-H, 2b-H, 3b-H, 6′b-H, 6′a-H, 5e-H), 3.62 (dd, $J_{2,3}$ = 10.1, $J_{3,4}$ = 3.6 Hz, 1 H, 3d-H), 3.65 (m, 1 H, 5f-H), 3.72−3.99 (m, 13 H, 6e-H, 6′e-H, 6c-H, 6′c-H, 6d-H, 4a-H, 6f-H, 6′f-H, 4e-H, 4c-H, 2e-H, 2c-H, 4b-H), 4.11−4.18 (m, 5 H, 4d-H, 3c-H, 3e-H, C*H*HPh, 6′d-H), 4.26−4.47 (m, 12 H, 1b-H, 1a-H, 1d-H, 4.5 C*H*$_2$Ph), 4.50 (d, J_{gem} = 12.0 Hz, 1 H, C*H*HPh), 4.53−4.57 (m, 2 H, C*H*$_2$Ph), 4.58 (d, $J_{1,2}$ = 10.3 Hz, 1 H, 1f-H), 4.63 (d, J_{gem} = 11.8 Hz, 1 H, C*H*HPh), 4.68 (d, J_{gem} = 10.9 Hz, 1 H, C*H*HPh), 4.70 (d, J_{gem} = 11.9 Hz, 1 H, C*H*HPh), 4.81−4.86 (m, 4 H, 1.5 C*H*$_2$Ph, 3f-H), 4.89 (d, J_{gem} = 10.5 Hz, 1 H, CH*H*Ph), 4.98 (d, J_{gem} = 12.4 Hz, 1 H, CH*H*Ph), 5.02 (d, J_{gem} = 11.3 Hz, 1 H, CH*H*Ph), 5.05 (d, $J_{1,2}$ = 8.4 Hz, 1 H, 1e-H), 5.08 (dd, $J_{1,2}$ = 7.9, $J_{2,3}$ = 10.1 Hz, 1 H, 2d-H), 5.15 (dd, $J_{1,2}$ = 8.0, $J_{2,3}$ = 12.4 Hz, 1 H, 2f-H), 5.17 (d, $J_{1,2}$ = 8.3 Hz, 1 H, 1c-H), 5.27 (d, $J_{3,4}$ = 4.0 Hz, 1 H, 4f-H), 5.40 (s, 1 H, C*H*Ph), 7.07−7.35 (m, 60 H, 12 Ph). − ^{13}C NMR (150.9 MHz, $CDCl_3$): δ = 55.50 (2e-C), 56.50 (2c-C), 61.10 (6f-C), 66.80 (5d-C), 67.20 (4f-C), 68.10 (6a-C), 68.40 (6c-C), 68.50 (6b-C, 6e-C), 68.80 (6d-C), 69.90 (2f-C), 70.90 (5f-C), 71.20 (3f-C, *C*H$_2$Ph), 73.30−76.00 (5b-C, 5c-C, 5a-C, 5e-C, 3d-C, 4d-C, 10 *C*H$_2$Ph), 76.30 (4a-C), 76.90 (4b-C), 77.70 (3c-C, 3e-C), 78.20 (4c-C), 78.50 (4e-C), 79.10, 82.50 (2b-C, 3b-C), 82.00, 83.40 (2a-C, 3a-C), 99.10 (1e-C), 100.10 (1c-C), 100.80 (1f-C), 101.00 (1d-C), 102.70 (1b-C), 102.80 (1a-C). − MALDI-MS (positive mode, DHB/THF matrix) *m*/*z*: 2516.5 [MNa$^+$]. − $C_{142}H_{152}N_2O_{38}$ (2494.66): calcd. C 68.36, H 6.14, N 1.12; found C 68.00, H 6.28, N 0.94.

Benzyl *O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-(3,6-di-*O*-benzyl-2-deoxy-2-dimethylmaleimido-β-D-glucopyranosyl)-(1→3)-(2-*O*-acetyl-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-β-D-glucopyranoside (12): A mixture of **11** (248 mg, 0.099 mmol), *p*-TsOH (4 mg, 0.021 mmol) and ethylmercaptan (50 mg, 0.804 mmol, 0.06 mL) in dry dichloromethane (1.5 mL) was stirred at room temp. After 24 h the mixture was neutralized by Et_3N and dried well in vacuo. The residue was purified by flash chromatography (ethyl acetate/petroleum ether, 1.25:1) to yield **12** (228 mg, 95%) as a white amorphous mass. − TLC (ethyl acetate/petroleum ether, 1.25:1): R_f = 0.19; $[\alpha]_D$ = −0.9 (*c* = 0.53, chloroform). − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.81, 1.83, 1.98, 2.01, 2.02, 2.08 (6 s, 27 H, 4 CH_3, 5 CH_3CO), 2.46 (br.s, 2 H, 2 OH), 2.97−5.18 (several signals, 63 H), 5.29 (d, $J_{3,4}$ = 3.3 Hz, 1 H, 4f-H), 7.07−7.38 (m, 55 H, 11 Ph). − MALDI-MS (positive mode, DHB/THF matrix) *m*/*z*: 2427.3 [MNa$^+$]. − $C_{135}H_{148}N_2O_{38}$ (2406.55): calcd. C 67.37, H 6.19 N1.16; found C 67.14, H 6.38, N 0.82.

Benzyl *O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-(2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-(2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (13): A mixture of **12** (228 mg, 0.094 mmol) and NaOH (600 mg, 15.0 mmol) in (MeOH/dioxane/H_2O, 5:1:1.7) was stirred at room temp. overnight. The reaction mixture was neutralized with 2 N HCl and then the pH was adjusted and kept at 5 with further 2 N HCl. After 24 h the solution was neutralized with ethanolamine and dried well in vacuo. The residue was treated with pyridine/acetic anhydride (15 mL) for 15 h and then worked up as described for **7**. The residue was purified by flash chromatography (ethyl acetate/petroleum ether, 1.5:1) and the partially unprotected fractions were collected and treated similarly as described above to give **13** (181 mg, 81%) as a white amorphous mass. − TLC (ethyl acetate/petroleum ether, 1.5:1): R_f = 0.16; $[\alpha]_D$ = −9.2 (*c* = 0.13, chloroform). − ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.48, 1.85, 1.90, 1.97, 1.99, 2.01, 2.04, 2.08 (8 s, 27 H, 9 CH_3CO), 3.04 (m, 1 H, 2e-H), 3.26 (m, 1 H, 5a-H), 3.35 (dd, 1 H, 6b-H), 3.41 (m, 1 H, 5b-H), 3.44 (m, 1 H, 2a-H), 3.50−3.58 (m, 6 H, 3a-H, 6′b-H, 5c-H, 5e-H, 5d-H, 3b-H), 3.64−3.75 (m, 10 H, 6a-H, 5f-H, 3d-H, 3c-H, 2b-H, 6′a-H, 6c-H, 6′c-H, 6e-H, 6′e-H), 3.82−3.84 (m, 2 H, 6d-H, 2c-H), 3.91−3.95 (m, 4 H, 4e-H, 4a-H, 6f-H, 4b-H), 3.94−4.05 (m, 3 H, 4c-H, 6′d-H, 6′f-H), 4.16−4.19 (m, 2 H, 3e-H, C*H*HPh), 4.31 (d, J_{gem} = 11.8 Hz, 1 H, C*H*HPh), 4.37 (d, J_{gem} = 12.1 Hz, 1 H, C*H*HPh), 4.40−4.76 (m, 18 H, 1b-H, 1d-H, 1a-H, 1f-H, 7 C*H*$_2$Ph), 4.83 (d, $J_{1,2}$ ≈ 7.4 Hz, 1 H, 1c-H), 4.87−5.01 (m, 6 H, 3f-H, 2.5 C*H*$_2$Ph), 5.07−5.16 (m, 4 H, 2d-H, 1e-H, 2f-H, 2c-NH), 5.31 (d, $J_{3,4}$ = 2.7 Hz, 1 H, 4f-H), 5.33 (d, $J_{3,4}$ = 2.9 Hz, 1 H, 4d-H), 5.63 (d, $J_{2,NH}$ = 7.2 Hz, 1 H, 2e-NH), 7.18−7.37 (m, 55 H, 11 Ph). − ^{13}C NMR (150.9 MHz, $CDCl_3$): δ = 54.80 (2c-C), 57.30 (2e-C), 61.10 (6f-C), 62.10 (6d-C), 67.10 (4f-C), 68.40 (6a-C), 68.60 (6b-C, 6c-C, 6e-C), 69.50 (4d-C), 69.80 (2f-C), 70.90 (5f-C), 71.20−77.10 (3f-C, 5d-C, 2d-C, 5b-C, 5c-C, 5e-C, 5a-C, 3d-C, 4c-C, 4a-C, 4e-C, 4b-C, 4e-C, 3e-C, 11 *C*H$_2$Ph), 78.90 (3c-C), 80.30 (2b-C), 82.00 (3b-C), 82.10 (2a-C), 83.20 (3a-C), 99.80 (1e-C), 100.30 (1d-C), 100.50 (1f-C), 102.30 (1c-C), 102.80 (1a-C), 103.00 (1b-C). − MALDI-MS (positive mode, DHB/THF matrix) *m*/*z*: 2382.4 [MNa$^+$]. − $C_{131}H_{148}N_2O_{37}$ (2342.51): calcd. C 67.16, H 6.36, N 1.19; found C 66.45, H 6.41, N 0.93.

(β-D-Galactopyranosyl)-(1→4)-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)-(β-D-galactopyranosyl)-(1→4)-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)-(β-D-galactopyranosyl)-(1→4)-α/β-D-glucopyranose (1b): A mixture of **13** (60 mg, 0.025 mmol) and NaOMe (0.195 M, 0.45 mL) in dry MeOH (6.85 mL) was stirred at room temp. After 7 h the reaction mixture was neutralized by

Amberlite IR 120 Resin (H^+form), filtered and dried well in vacuo to give intermediate **14**. − TLC (acetone/toluene, 2:1): $R_f = 0.3$. The afore-mentioned intermediate was dissolved in (MeOH/AcOH/dioxane, 1:1:1−3 mL) and hydrogenated in the presence of Pd-C (10%Pd, 0.03 g). After 3 d the mixture was filtered through celite, washed with (EtOH/H_2O, 1:1) and the filtrate was evaporated in vacuo. The residue was purified by flash chromatography NH_2-phase (EtOH/H_2O, 3:1) to yield **1b** (260 mg, qu). − TLC NH_2-Phase (EtOH/H_2O, 3:1): $R_f = 0.29$. − MALDI-MS (positive mode, DHB/H_2O matrix) *m*/*z*: 1094.8 [MNa^+]. $C_{40}H_{68}N_2O_{31}$ (1072.96).

Acetyl *O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α/β-D-glucopyranoside (15): A mixture of **1b** (43o mg, 0.04 mmol), pyridine (10 mL) and acetic anhydride (5 mL) was stirred at room temp. After 24 h the reaction mixture was worked up as described for **13**. The residue was purified by flash chromatography (toluene/acetone, 1:1.25) to yield **15** (50 g, 68%) as a white powder in the ratio of α,β = 1:1.27 . − TLC (toluene/acetone, 1:1.25). $R_f = 0.16$. − ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.89−2.17 (many s, 20 CH_3CO), 3.49−3.53 (m, 4 H, 5c-H, 5e-H, 2e-H, 2c-H), 3.72−3.78 (m, 7.56 H, 3b-H, 3d-H, 4c-H, $4a_\alpha$-H, 5d-H, 5b-H, $5a_\beta$-H, $4a_\beta$-H, 5a-H, 4e-H), 3.86 (br.t, 1 H, 5f-H), 3.94−3.97 (m, 2.44 H, 6e-H, 6c-H, $5a_\alpha$-H), 4.03−4.13 (m, 7 H, 6b-H, 6′b-H, 6d-H, 6′d-H, 6f-H, 6′f-H, $6a_\alpha$-H, $6a_\beta$-H), 4.32, 4.33 (2 d, $J_{1,2}$ = 9.7 Hz, 1 H, $1b_\beta$-H, $1b_\alpha$-H), 4.39, 4.40 (m, 1 H, $6'a_\alpha$-H, $6'a_\beta$-H), 4.40 (d, $J_{1,2}$ = 7.7 Hz, 1 H, 1d-H), 4.53 (d, $J_{1,2}$ = 7.9 Hz, 1 H, 1f-H), 4.63 (2 d, $J_{1,2}$ = 7.7, 8.0 Hz, 1 H, 1c-H), 4.69 (d, $J_{1,2}$ = 7.5 Hz, 1 H, 1e-H), 4.72−4.77 (m, 2 H, 6c-H, 6e-H), 4.97−5.03 (m, 4 H, 3f-H, 2b-H, 2d-H, $2a_\alpha$-H, $2a_\beta$-H), 5.10−5.20 (m, 3.56 H, 2f-H, 3c-H, 3e-H, $3a_\beta$-H), 5.29−5.30 (m, 2 H, 4d-H, 4b-H), 5.33 (br.s, 3 H, 2c-NH, 2e-NH, 4f-H), 5.42 (t, $J_{2,3} = J_{3,4}$ = Hz, 0.44 H, $3a_\alpha$-H), 5.65 (d, $J_{1,2}$ = 8.2 Hz, 0.56 H, $1a_\beta$-H), 6.24 (d, $J_{1,2}$ = 3.5 Hz, 0.44 H, $1a_\alpha$-H). − ^{13}C NMR (150.9 MHz, $CDCl_3$): δ = 20.48−29.66 (20 $\mathit{C}H_3CO$-C),54.80 (2c-C), 55.00 (2e-C), 60.20 (6e-C), 60.50 (6c-C), 60.70 (6f-C), 61.50 (6b-C, $6a_\alpha$-C), 61.60 (6d-C), 61.80 ($6a_\beta$-C), 66.60 (4f-C), 68.80 (4b-C), 69.10 (2f-C), 69.30 ($3a_\alpha$-C, $2a_\alpha$-C), 70.40 ($2a_\beta$-C), 70.60 (5f-C), 70.80 ($5a_\alpha$-C), 71.00 (2b-C, 2d-C), 71.10 (5d-C, 5b-C, $5a_\beta$-C), 71.70 (3c-C), 71.80 (3e-C), 72.30 ($3a_\beta$-C), 72.60 (5c-C, 5e-C), 73.60 ($4a_\alpha$-C), 75.00 (4e-C), 75.20 (4c-C), 75.60 ($4a_\beta$-C), 75.70 (3b-C, 3d-C), 88.95 ($1a_\alpha$-C), 91.50 ($1a_\beta$-C), 100.20 (1e-C), 100.30 (1c-C), 100.50, 100.80 (1b-C), 100.70 (1d-C), 101.80 (1f-C), 168.95−170.62 (20 $CH_3\mathit{C}O$-C). − $C_{76}H_{104}N_2O_{49}$ (1829.60).

Benzyl *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-β-D-glucopyranoside (17): A mixture of **16**[4] (428 mg, 0.244 mmol), dry MeOH (4.6 mL) and NaOMe (0.195 M, 0.26 mL) was stirred at room temp. After 2 h the reaction mixture was worked up as described for **2**. The residue was purified by flash chromatography (toluene/acetone, 5:3) to yield **17** (330 mg, 85%) as a white foam. − TLC (toluene/acetone, 5:3): $R_f = 0.11$; $[\alpha]_D$ = − 1.0 (*c* = 0.46, chloroform). − ^{1}HNMR (250 MHz, $CDCl_3$): = 1.23−1.63 (br.m, 6 H, 2 CH_3), 2.67 (m, 4 H, 4 OH), 2.98−5.24 (m, 46 H), 7.04−7.32 (m, 45 H, 9 Ph). − MALDI-MS (positive mode, DHB/THF matrix) *m*/*z*:1609.8 [MNa^+]. − $C_{93}H_{101}NO_{22}$ (1584.74): calcd. C 70.48, H 6.42, N 0.88; found C 70.08, H 6.60, N 0.58.

Benzyl *O*-(4,6-*O*-Benzylidene-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-β-D-glucopyranoside (18): A mixture of **17** (0.33 g, 0.2 mmol), *p*-TsOH (6 mg, 0.031 mmol) and benzaldehyde dimethylacetal (152 mg, 0.999 mmol, 0.15 mL) in dry acetonitrile was stirred at room temp. After 14 h the reaction mixture was neutralized by Et_3N and dried well in vacuo. The residue was purified by flash chromatography (petroleum ether/ethyl acetate, 1:1) to yield **18** (285 mg, 81%) as a white foam. − TLC (petroleum ether/ethyl acetate, 1:1): $R_f = 0.11$; $[\alpha]_D = -2.4$ (*c* = 0.53, chloroform). − ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.25−1.57 (br.m, 6 H, 2 CH_3), 2.42 (d, $J_{3,OH}$ = 9.0 Hz, 1 H, 3d-OH), 2.99 (m, 1 H, 5a-H), 3.09 (m, 1 H, 5d-H), 3.13 (d, $J_{2,OH}$ = 2.2 Hz, 1 H, 2d-OH), 3.35−3.39 (m, 5 H, 6b-H, 6a-H, 5b-H, 2a-H, 3a-H), 3.48 (dd, $J_{2,3} = J_{3,OH}$ = 9.0 Hz, $J_{3,4}$ = 3.8 Hz, 1 H, 3d-H), 3.51−3.53 (m, 3 H, 6′b-H, 2b-H, 3b-H), 3.56 (dd, J_{gem} = 11.1, $J_{5,6'}$ = 4.0 Hz, 1 H, 6′a-H), 3.54 (m, 1 H, 5c-H), 3.69 (br.t, 1 H, 2d-H), 3.80 (dd, J_{gem} = 11.3, $J_{5,6}$ = 1.9 Hz, 1 H, 6c-H), 3.86−3.88 (m, 2 H, 6d-H, 4a-H), 4.00 (d, $J_{3,4}$ = 1.8 Hz, 1 H, 4b-H), 4.07−4.17 (m, 6 H, 2c-H, 4d-H, 6′c-H, 4c-H, 6′d-H, C*H*HPh), 4.27 (d, J_{gem} = 12.2 Hz, 1 H, C*H*HPh), 4.30−4.36 (m, 5 H, 3c-H, 1b-H, 1a-H, 2 C*H*HPh), 4.44−4.50 (m, 5 H, 2.5 $C\mathit{H}_2$Ph), 4.55−4.60 (m, 3 H, 1d-H, $C\mathit{H}_2$Ph), 4.63 (d, J_{gem} = 11.8 Hz, 1 H, CH*H*Ph), 4.69 (d, J_{gem} = 10.8 Hz, 1 H, C*H*HPh), 4.85 (d, J_{gem} = 10.4 Hz, 1 H, CH*H*Ph), 4.86 (d, J_{gem} = 11.2 Hz, 1 H, CH*H*Ph), 4.92 (d, J_{gem} = 10.5 Hz, 1 H, CH*H*Ph). 5.01 (d, J_{gem} = 12.4 Hz, 1 H, CH*H*Ph), 5.04 (d, *J*gem = 11.4 Hz, 1 H, CH*H*Ph), 5.22 (d, $J_{1,2}$ = 8.4 Hz, 1 H, 1c-H), 5.46 (s, 1 H, C*H*Ph), 7.09−7.32 (m, 50 H, 10 Ph). − ^{13}C NMR (150.9 MHz, $CDCl_3$): δ = 56.34 (2c-C), 66.53 (5d-C), 67.74 (6a-C), 68.21 (6b-C), 68.58 (6c-C), 68.924 (6d-C), 70.82 ($\mathit{C}H_2$Ph-C), 72.48 (2d-C), 72.83−75.41 (3d-C, 5b-C, 5c-C, 5a-C, 4d-C, 8 $\mathit{C}H_2$Ph), 76.01 (4a-C), 76.60 (4b-C), 78.28 (3c-C), 78.40 (4c-C), 78.88 (2b-C), 81.66 (2a-C), 82.01 (3b-C), 83 (3a-C), 99.97 (1c-C), 101.32 (*C*HPh-C), 102.35 (1b-C), 102.42 (1a-C), 102.94 (1d-C), 128.38−139.05 (10 Ph-C). − MALDI-MS (positive mode, DHB/THF matrix) *m*/*z*: 1696.5 [MNa^+], 1713.5 [MK^+] . − $C_{100}H_{105}NO_{22}$ (1672.84): C 71.79, H 6.32, N 0.83; found C 71.55, H 6.51, N 0.62.

Benzyl *O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-(3,6-di-*O*-benzyl-2-deoxy-2-dimethylmaleimido-β-D-glucopyranosyl)-(1→3)-(2-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-(3,6-di-*O*-benzyl-2-deoxy-2-dimethylmaleimido-β-D-glucopyranosyl)- (1→3)-(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-β-D-glucopyranoside (20): A mixture of **9** (200 mg, 0.118 mmol) and **18** (0.095 mmol) in dry acetonitrile (1 mL) was stirred under nitrogen at − 30°C while TMSOTf (0.01 M in acetonitrile, 0.11 mL) was added dropwise. After 45 min the reaction mixture was neutralized by Et_3N and evaporated in vacuo. The residue was purified by MPLC (petroleum ether/ethyl acetate, 1:1) to yield **19** (170 mg, 55%) as a white amorphous mass. − TLC (petroleum ether/ethyl acetate, 1:1): R_f = 0.18. A mixture of **19** (170 mg, 0.53 mmol), *p*-TsOH (0.008 g, 0.042 mmol) and ethylmercaptan (117 mg, 1.892 mmol, 0.14 mL) in dry acetonitrile (3 mL) was stirred under nitrogen at room temp. After 17 h the reaction mixture was neutralized by Et_3N and dried well in vacuo. The residue was purified by flash chromatography (toluene/acetone, 2:1) to yield **20** (115 mg, 71%) as an amorphous white mass. − TLC (toluene/acetone, 2:1): R_f = 0.23; $[\alpha]_D$ = + 1.0 (*c* = 0.6, chloroform). − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.76, 1.80, 1.84, 1.98, 2.01, 2.02, 2.08 (7 s, 33 H, 5 CH_3CO, 6 CH_3), 2.40−2.54 (m, 5 H, 5 OH), 3.22−5.19 (m, 81 H), 5.29 (d, $J_{3,4}$ = 3.7 Hz, 1 H, 4 h-H), 7.07−7.38 (m, 65 H, 13 Ph). − MALDI-MS (positive mode, DHB/THF matrix) *m*/*z*: 3040.5 [MNa^+]. − $C_{167}H_{185}N_3O_{49}\cdot 3H_2O$ (3072.21): calcd. C 65.28, H 6.26, N 1.36; found C 65.13, H 6.32, N 1.21.

Benzyl *O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-(2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-(2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-(2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (21): Compound **20** (115 mg, 0.038 mmol) was treated with NaOH, HCl and then with Ac_2O/Pyr as described for **12**. The residue was purified by MPLC (toluene/acetone, 3:1) to yield **21** (840 mg, 73%) as a white amorphous mass. − TLC (toluene/acetone, 3:1): $R_f = 0.12$; $[\alpha]_D = - 3.0$ ($c = 0.2$, chloroform). − ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.84, 1.85, 1.90, 1.92, 1.95, 1.97, 1.99, 2.01, 2.04, 2.06, 2.08 (11 s, 39 H, 13 CH_3CO), 3.02 (m, 1 H, 2 g-H), 3.10 (m, 1 H, 2e-H), 3.25 (m, 1 H, 5a-H), 3.34 (m, 1 H, 6b-H), 3.41 (m, 1 H, 5b-H), 3.44 (m, 1 H, 2a-H), 3.49−3.59 (m, 8 H, 6′b-H, 3a-H, 5d-H, 5e-H, 5 g-H, 5c-H, 3b-H, 5f-H), 3.64−3.74 (m, 13 H, 6a-H, 5 h-H, 3d-H, 3c-H, 2b-H, 3f-H, 6′a-H, 6e-H, 6′e-H, 6 g-H, 6′g-H, 6c-H, 6′c-H), 3.81−4.19 (m, 15 H, 6d-H, 6f-H, 2c-H, 4e-H, 4 g-H, 4b-H, 4a-H, 4c-H, 6 h-H, 6′d-H, 6′h-H, 6′f-H, 3e-H, 3 g-H, C*H*HPh), 4.30−4.99 (m, 32 H, 12.5 CH_2Ph, 1b-H, 1d-h, 1a-H, 1f-H, 1 h-H, 1c-H, 3 h-H), 5.05−5.15 (m, 6 H, 1e-H, 2d-H, 2f-H, 1 g-H, 2 h-H, 2c-NH), 5.30 (d, $J_{3,4} = 2.9$ Hz, 1 H, 4 h-H), 5.32 (d, $J_{3,4} = 2.9$ Hz, 1 H, 4d-H), 5.34 (d, $J_{3,4} = 2.8$ Hz, 1 H, 4f-H), 5.62 (d, $J_{2,NH} = 7.3$ Hz, 1 H, 2 g-NH), 5.66 (d, $J_{2,NH} = 7.3$ Hz, 1 H, 2e-NH), 7.18−7.35 (m, 65 H, 13 Ph). − ^{13}C NMR (150.9 MHz, $CDCl_3$): δ = 54.50 (2c-C), 56.30 (2e-C), 57.00 (2 g-C), 60.80 (6 h-C), 61.80 (6d-C), 61.90 (6f-C), 66.90 (4 h-C), 68.10 (6a-C), 68.20 (6b-C), 68.50 (6e-C, 6 g-C, 6c-C), 69.20 (4d-C, 4f-C), 69.40 (2 h-C), 70.60−76.70 (5 h-C, 3 h-C, 2d-C, 2f-C, 13 *C*H_2Ph-C, 5c-C, 5f-C, 5b-C, 5d-C, 5e-C, 5 g-C, 5a-C, 3f-C, 3d-C, 4c-C, 4b-C, 4e-C, 4 g-C, 4a-C, 3e-C, 3 g-C), 78.50 (3c-C), 80.00 (2b-C), 81.60 (3b-C), 81.70 (2a-C), 82.90 (3a-C), 99.50 (1 g-C), 99.60 (1e-C), 99.90 (1d-C), 100.10 (1 h-C, 1f-C), 102.00 (1c-C), 102.40 (1a-C), 102.60 (1b-C). − MALDI-MS (positive mode, DHB/THF matrix) *m*/*z*: 3056.4 [MNa+]. − $C_{165}H_{189}N_3O_{51}$ (3030.186): calcd. C 65.39, H 6.28, N 1.38; found C 65.59, H 6.80, N 1.27.

***O*-(β-D-Galactopyranosyl)-(1→4)-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)-(β-D-galactopyranosyl)-(1→4)-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)-(β-D-galactopyranosyl)-(1→4)-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)-(β-D-galactopyranosyl)-(1→4)-(α/β-D-glucopyranose (1c):** A mixture of **21** (460 mg, 15.1 µmol) and NaOMe (0.195 M, 0.45 mL) in dry MeOH (6.85 mL) was stirred at room temp. After 8 h the reaction mixture was neutralized with Amberlite IR 120 Resin (H^+form), filtered and dried well in vacuo. The residue was dissolved in 4 mL MeOH/AcOH (1:1) and hydrogenated in the presence of Pd/C (10%Pd, 30 mg). After three days the mixture was filtered through celite, washed with EtOH/H_2O (2:1) and the filtrate was evaporated to dryness in vacuo. The residue was purified by flash chromatography NH_2-phase (EtOH/H_2O, 2:1) to yield **1c** (210 mg, 100%). − TLC NH_2-phase (EtOH/H_2O, 2:1): $R_f = 0.52$. − MALDI-MS (positive mode, DHB/H_2O matrix) *m*/*z*: 1462.6 [MNa^+]; $C_{54}H_{91}N_3O_{41}$ (1438.29).

Acetyl *O*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)- (2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α/β-D-glucopyranoside (22): A mixture of **1c** (110 mg, 7.6 µmol), pyridine (10 mL) and acetic anhydride (5 mL) was stirred at room temp. After two days the reaction mixture was worked up as described for **13**. The residue was purified by flash chromatography (toluene/acetone, 1:2) to yield **22** (150 mg, 83%) as a white powder in the ratio α.β = 2:3. − TLC (toluene/acetone, 1:2): $R_f = 0.16$. − ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.89−2.18 (many s, 78 H, 26 CH_3CO), 3.50−4.14 (m, 30 H), 4.34 (d, $J_{1,2} = 8.0$ Hz, 1 H, 1b-H), 4.42 (d, $J_{1,2} = 9.7$ Hz, 2 H, 1d-H, 1f-H), 4.40−4.41 (m, 1 H), 4.55 (d, $J_{1,2} = 9.7$ Hz, 1 H, 1h-H), 4.64, 4.67, 4.69 (3 d, $J_{1,2} = 9.7$ Hz, 3 H, 1c-H, 1e-H, 1 g-H), 4.68−4.73 (m, 3 H), 5.04−5.43 (m, 14 H), 5.66 (d, $J_{1,2} = 8.2$ Hz, 0.6 H, $1a_\beta$-H), 6.25 (d, $J_{1,2} = 3.5$ Hz, 0.4 H, $1a_\alpha$-H). − $C_{100}H_{137}N_3O_{64}$ (2406.12).

Acknowledgments

This work was supported by the European Community (Grant N° FAIR-CT97−3142), the Bundesministerium für Bildung und Forschung (Grant N° 0311 229), and the Fonds der Chemischen Industrie. M.R.E.A. is grateful for a stipend within the channel program of the Egyptian Government. The help of Dr. Armin Geyer in structural assignments is gratefully acknowledged.

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Received August 11, 1999
[O99495]