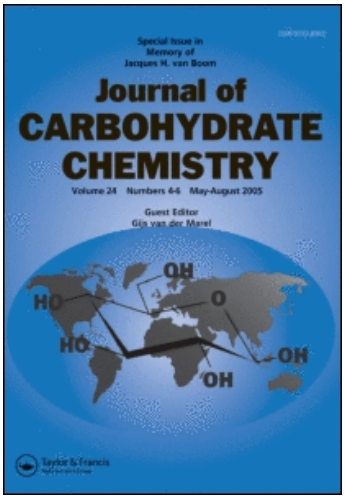


Journal of Carbohydrate Chemistry

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

Synthesis of Oligosaccharides Designed to form Micelles, Corresponding to Structures Found in Ovarian Cyst Fluid

Therese Buskas; Peter Konradsson

To cite this Article Buskas, Therese and Konradsson, Peter(2000) 'Synthesis of Oligosaccharides Designed to form Micelles, Corresponding to Structures Found in Ovarian Cyst Fluid', Journal of Carbohydrate Chemistry, 19: 1, 25 — 51

To link to this Article: DOI: 10.1080/07328300008544063

URL: http://dx.doi.org/10.1080/07328300008544063

J. CARBOHYDRATE CHEMISTRY, 19(1), 25–51 (2000)

SYNTHESIS OF OLIGOSACCHARIDES DESIGNED TO FORM MICELLES, CORRESPONDING TO STRUCTURES FOUND IN OVARIAN CYST FLUID

Therese Buskas[a] and Peter Konradsson[b]*

[a]Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, S-106 91 Stockholm, Sweden
[b]Department of Chemistry, University of Linköping, S-581 83 Linköping, Sweden

Received April 1, 1999 - Final Form October 29, 1999

ABSTRACT

The syntheses of α-D-Glc*p*NAc-(1→4)-β-D-Gal*p*-(1→4)-β-D-GlcNAc-(1→O)-$(CH_2)_{15}CH_3$ (**1**) and fragments thereof, corresponding to structures found in human ovarian cyst fluid, are described. Silver triflate promoted coupling of 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-β-D-glucopyranosyl bromide (**12**) and galactose acceptor (**11**) gave a disaccharide donor (**13**), which was readily transformed into the corresponding bromo-derivative **18**. For the synthesis of disaccharide β-D-Gal*p*-(1→4)-D-GlcNAc, several differently protected glucosamine acceptors were prepared. It was found that cetyl alcohol needed to be introduced after the formation of the β-galactoside bond. Glycosylation of pent-4-enyl 3,6-di-*O*-benzyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside (**30**) with (3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-(1→4)-2,3,6-tri-*O*-benzoyl-α-D-galactopyranosyl bromide (**18**) by use of silver triflate as promoter gave the desired trisaccharide **31**. Finally **31** was transformed *via* coupling to the long alkyl chain aglycon and deprotection into the title compound **1**.

INTRODUCTION

The oligosaccharide 2-acetamido-2-deoxy-α-D-glucopyranosyl-(1→4)-β-D-galacto-pyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranose has been identified in human ovarian cyst fluid[1-3] and foetal gastrointestinal mucins.[4] So far the structure has been suggested to be a tumour marker and antibodies raised against seminal fluids bind to the trisaccharide. Nonetheless, the function and origin of the component is still unclear and to facilitate biological studies synthetic substances were desirable.

The trisaccharide **1** (Fig 1) was previously synthesised by Paulsen *et al.* in its free pyranose form.[5] Our objective was to design a synthesis with flexibility to give not only the trisaccharide **1** as a target molecule, but also the two possible disaccharide units (**3** and **5**). Another desirable feature in the synthetic strategy was to build in the ability to isolate the final products with the amino functions either as the naturally occurring *N*-acetamido derivatives or as the free amines (**2**, **4** and **6**).

Instead of preparing *neo*-glycoconjugates, it was desirable to use synthetic liposomes (micelles) for the biological studies. The use of simple alkyl chains (C_{16} or C_8) as aglycons was chosen to ensure that liposomes (micelles) would form easily.[6] Amphiphilic molecules, like these alkyl glycosides, can form a variety of different liquid crystalline phases such as micelles and cubic phases. The cubic phase is of special interest, since there is some evidence that it might play a vital role in biological processes like membrane fusion and endocytosis.[7]

RESULTS AND DISCUSSION

Synthesis of the building block corresponding to the terminal end disaccharide, 2-acetamido-2-deoxy-α-D-glucopyranosyl-(1→4)-β-D-galactopyranose, was performed first. Formation of the glycosidic linkage in this unit appeared to be more challenging than that of the β-Gal*p*-(1→4)-GlcNAc, and so it was desirable to make it at an early stage in the synthesis.

A simple four step route, based on the synthetic pathway to 3,4-diols of galactosides reported by Garegg *et al.*,[8] was employed (Scheme 1) for preparation of the galactose building block. Starting from ethylthio galactoside **7**[9,10] the 3,4-*O*-isopropylidene derivative **8** was prepared with high regioselectivity and was isolated, after standard benzoylation of the 2,6-positions, in 76% yield. Removal of the isopropylidene group using 90% aqueous trifluoroacetic acid (TFA) gave diol **10** in 80% yield which, by

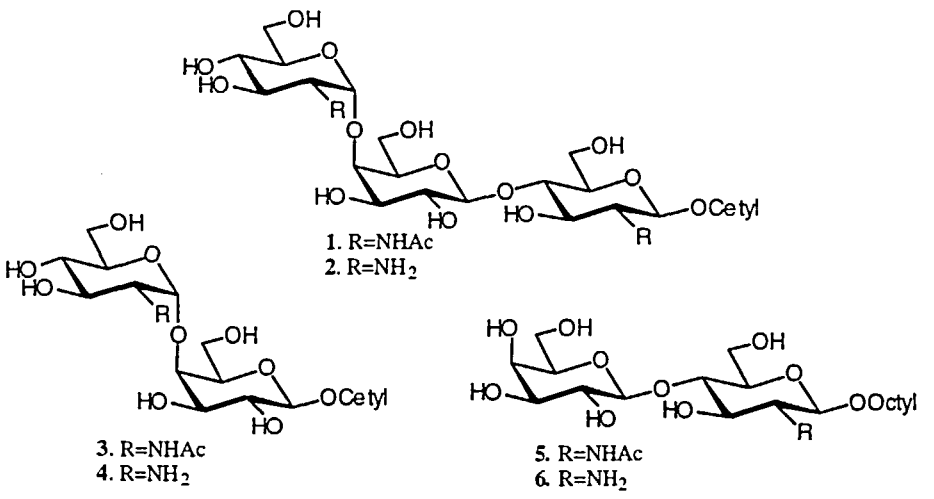
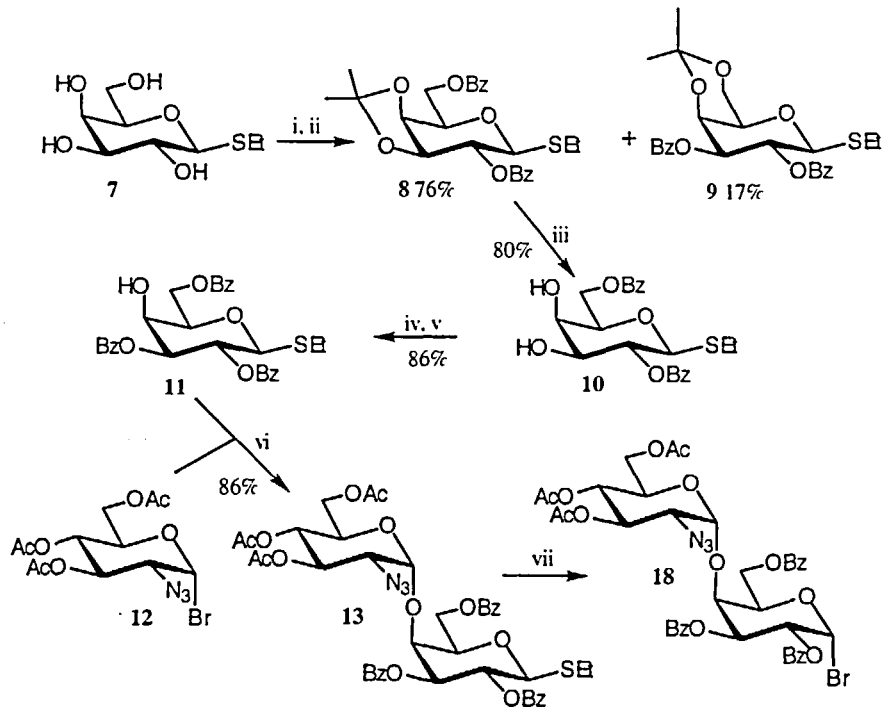


Figure 1

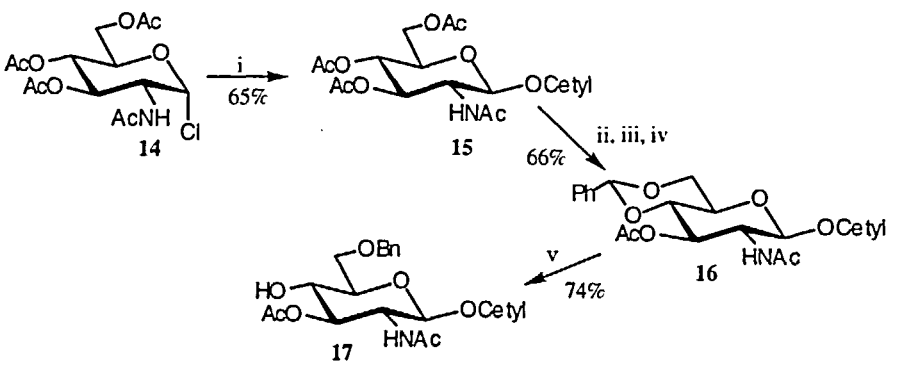
stannylidene assisted selective benzoylation,[11-13] was transformed to the ready acceptor **11** (86%).

A donor with the non-participating 2-azido-2-deoxy group was chosen in order to perform an efficient α-selective glycosylation. Using the diazotransfer methodology[14-16] and starting from glucosamine hydrochloride,[17] the donor 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl bromide **12**[18] was synthesised by known techniques. Silver triflate[19] (AgOTf) promoted glycosylation with donor **12** and acceptor **11** then gave the desired disaccharide **13** in 86% yield (Scheme 1). Some preliminary studies indicated that the same donor with benzyl groups in place of the acetyl groups was inferior in glycosylations with 4-OH-galactose acceptors. The reactivities of the reactants were poorly matched and the donor decomposed rapidly.

Several different derivatives were examined as building blocks for the glucosamine at the reducing end. Initially, the aglycon was introduced prior to the other sugar residues. In the synthesis outlined in Scheme 2, glycosyl chloride **14**[20] was coupled to cetyl alcohol under Helferich conditions[21] to produce glycoside **15** in 65% yield. Three standard operations, deacetylation, 4,6-*O*-benzylidenation and acetylation performed on **15** gave compound **16** in 66% overall yield. However, severe solubility problems were encountered during these transformations which, despite the yield, made the method somewhat inconvenient. Reductive opening of the 4,6-*O*-benzylidene acetal using sodium cyanoborohydride and anhydrous HCl in diethyl ether[22] was straightforward and produced the acceptor **17** in 74% yield.



Scheme 1 **i**: Acetone, *p*TsOH; **ii**: BzCl, pyridine; **iii**: 90% TFA aq.; **iv**: $(Bu)_2SnO$, MeOH, reflux; **v**: BzCl, TEA, THF; **vi**: AgOTf, *sym*-collidine, CH_2Cl_2, -30°C; **vii**: Br_2, CH_2Cl_2.



Scheme 2 **i**: $CH_3(CH_2)_{14}CH_2OH$, $Hg(CN)_2$, $HgBr_2$, toluene, Drierite; **ii**: 1M NaOMe, MeOH; **iii**: α,α-dimethoxytoluene:DMF 1:1, *p*TsOH, 50 °C; **iv**: Ac_2O, pyridine; **v**: $NaBH_3CN$, HCl/Et_2O, THF

Unfortunately, all attempts to glycosylate this acceptor (**17**) failed. Disaccharide donor **18** (Scheme 1), prepared by treatment of thioglycoside **13** with bromine just prior to coupling,[23,24] gave no desired trisaccharide product in silver triflate promoted coupling reactions in dichloromethane as seen in Table 1, entry 1. The outcome was the same if the anomeric leaving group of the donor was changed into fluoride[25] or trichloroacetimidate,[26,27] as was the use of the thioglycoside **13** in dimethyl(methylthio)sulfonium triflate (DMTST)[28] promoted reactions. Two possible explanations for these poor results came first to mind, low solubility of the acceptor due to the long lipophilic alkyl chain or the influence of the 3-*O*-acetyl as protecting group. A number of different acceptors were therefore prepared to examine these effects (see Scheme 3 and Table 1).

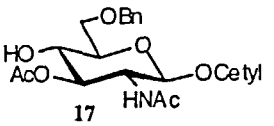
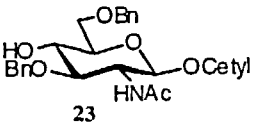
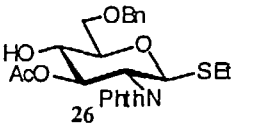
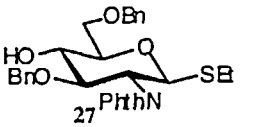
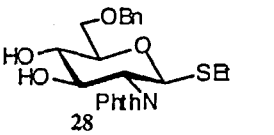
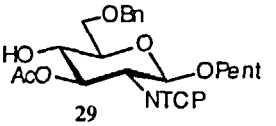
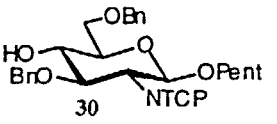
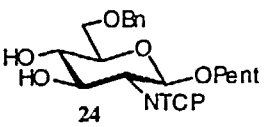
As introduction of a benzyl group in place of the acetyl group would hopefully produce a more reactive acceptor than **17**, 3-*O*-benzylated acceptors were prepared as cetyl (**23**), ethylthio (**27**)[29] or *n*-pentenyl (**30**)[30] glycosides, respectively. Preparation of cetyl derivative **23** was conveniently done using tetrachlorophthalimido (TCP) protected *n*-pentenyl glycosides as precursors. The cetyl alcohol was coupled to donor **20**[30] in an *N*-iodosuccinimide/triethylsilyl triflate[31,32] (NIS/TESOTf) promoted reaction to give the alkyl glycoside **21** (68%) (Scheme 3). Acceptor **23** was then prepared by reductive opening of the benzylidene acetal of **21** (70%) followed by removal of the TCP group, *O*- and *N*-acetylation and Zemplén deacetylation (87%).

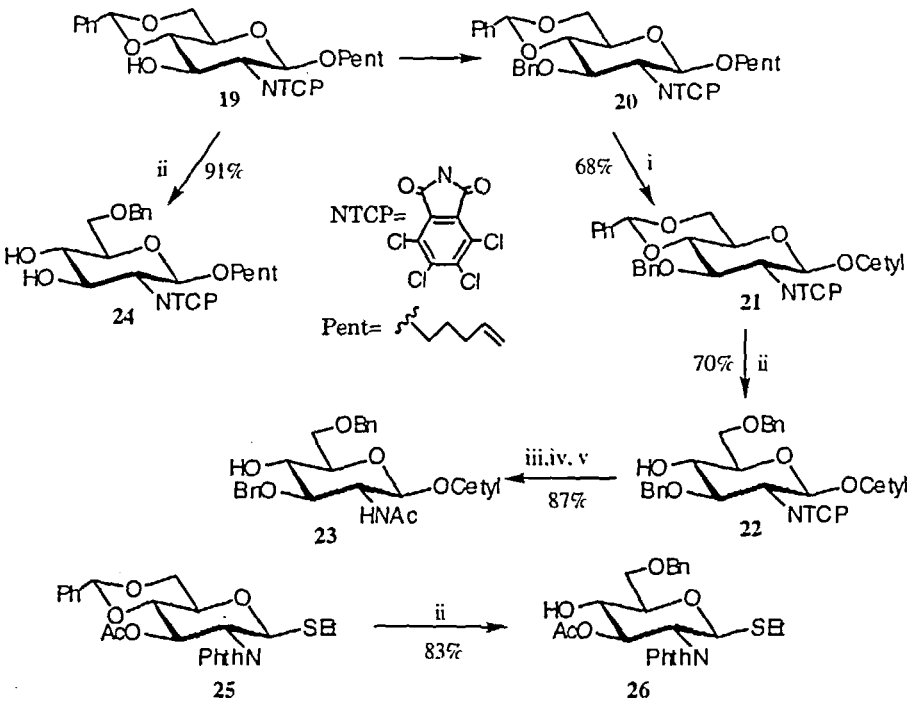
To be able to make this study more conclusive ethylthio and *n*-pentenyl acceptors were also prepared as 3-*O*-acetyl derivatives **26** and **29**[33] as well as the 3,4-diols **24** and **28**.[34] Synthesis of **24** and **26** was achieved in 91% and 83% by reductive ring opening of the benzylidene acetal of **19**[30] and **25**,[24] respectively (Scheme 3).

Glycosylation of the various acceptors with disaccharide donor **18** in silver triflate promoted reactions are summarised in Table 1. It can be concluded that glycosylation was impossible when the 3-*O*-acetyl was present (entries 1, 3 and 6) regardless of the anomeric substituent. Introduction of a 3-*O*-benzyl gave the desired improvement in reactivity for the thio and *n*-pentenyl acceptors (entries 4 and 7) with a most encouraging yield of 87% of trisaccharide **31** for the latter (Scheme 4). In contrast, the 3-*O*-benzylated cetyl glycoside **23** (entry 2) gave no trisaccharide product and the strategy of introducing the aglycon at an early stage could therefore be ruled out.

Several regioselective β 1→4-glycosylations of *N*-protected glucosamine derivatives have been reported in the literature.[34-43] Here condensation of donor **18** and the 3,4-diol acceptors **28** and **24** (Table 1, entries 5 and 8) using silver triflate as promoter at –30 °C gave the β 1→4 linked compounds **33** and **34** (Figure 2) in 68 and 78% yield, respectively. The new structures were confirmed by performing two-dimensional nuclear

Table 1. Glycosylations of various glucosamine acceptors using donor **18**. Reaction conditions: *donor 1 equiv, AgOTf 2 equiv, acceptor 1.1 equiv, 3Å Ms, dry* CH_2Cl_2. a). No product could be isolated. The acceptor was recovered in almost quant. yield. b). 70% of the acceptor was recovered together with a complex mixture of products. c). *See figure 2.* d) *See scheme 4.*

Entry	Acceptor	temp °C	product (yield%)
1.	 **17**	-30 - 0	a
2.	 **23**	-30 - 0	b
3.	 **26**	-30 - 0	a
4.	 **27**	-30	**32** (57%)[c]
5.	 **28**	-30	**33** (68%)[c]
6.	 **29**	-30 - 0	a
7.	 **30**	-30	**31** (87%)[d]
8.	 **24**	-30	**34** (78%)[c]

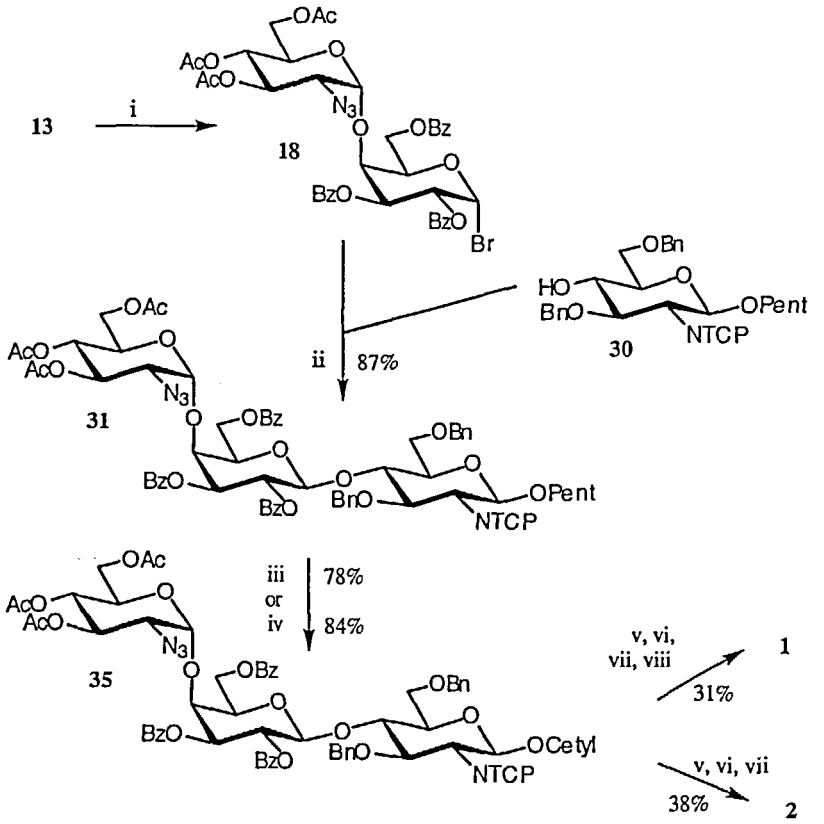


Scheme 3 **i**: $CH_3(CH_2)_{14}CH_2OH$, NIS, TESOTf, CH_2Cl_2; **ii**: $NaBH_3CN$, HCl/Et_2O, THF; **iii**: ethylenediamine, EtOH:dioxane 1:1, 70 °C; **iv**: Ac_2O, pyridine; **v**: 1M NaOMe, MeOH

Overhauser enhancement NMR spectroscopy. No β 1→3 linked compounds were isolated. The overall yields in these selective couplings were comparable to the use of 3-*O*-benzylated derivatives. However, in our overall strategy the presence of a free hydroxyl group on the trisaccharide could later become a disadvantage so the use of a 3-*O*-benzylated acceptor was preferable for this work. Use of *n*-pentenyl acceptor **30** as building block for the reducing end glucosamine for further synthesis was a simple choice.

The coupling with donor **18** was high yielding (Scheme 4). preparation was straightforward. and the *n*-pentenyl group can be directly activated for further glycosylations[31,32] or be transformed to a variety of spacers.[44]

Cetyl alcohol was coupled to trisaccharide **31** in a NIS/TESOTf promoted reaction to produce the fully protected alkyl derivative **35** in 78% yield (Scheme 4). The promoter pair NIS/AgOTf[31,32] was also tried as a coupling reagent and gave a comparable yield (84%). The protecting groups were then removed in three steps. Ethylenediamine treatment removed the TCP group[30] and was followed by deacylation under Zemplén conditions.[45]



Scheme 4 **i**: Br_2, CH_2Cl_2; **ii**: AgOTf, *sym*-collidine, CH_2Cl_2, -30 °C; **iii**: $CH_3(CH_2)_{14}CH_2OH$, NIS, TESOTf, CH_2Cl_2; **iv**: $CH_3(CH_2)_{14}CH_2OH$, NIS, AgOTf, CH_2Cl_2; **v**: ethylenediamine, CH_3CN:EtOH:THF 2:1:1, 60 °C; **vi**: 1M NaOMe, MeOH; **vii**: H_2/Pd; **viii**; Ac_2O, MeOH

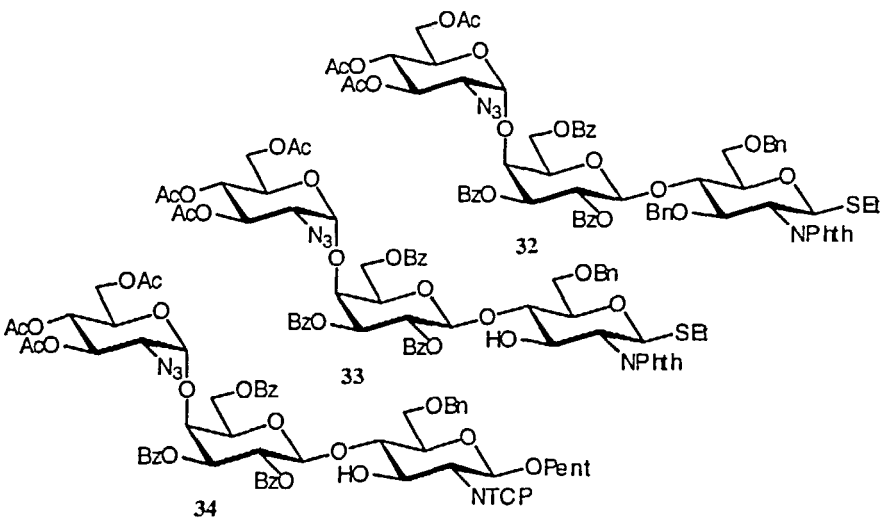
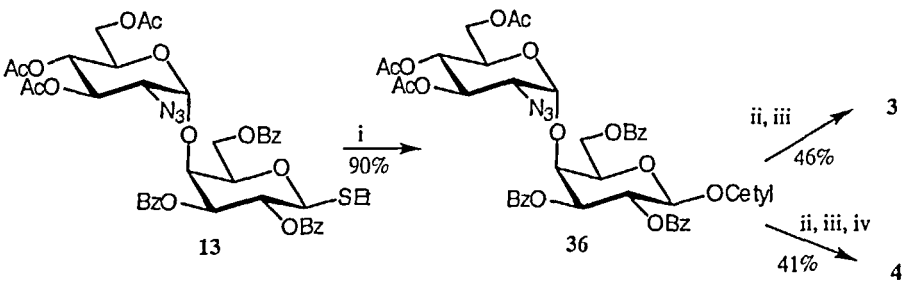


Figure 2. Products obtained in the glycosylation study outlined in table 1.



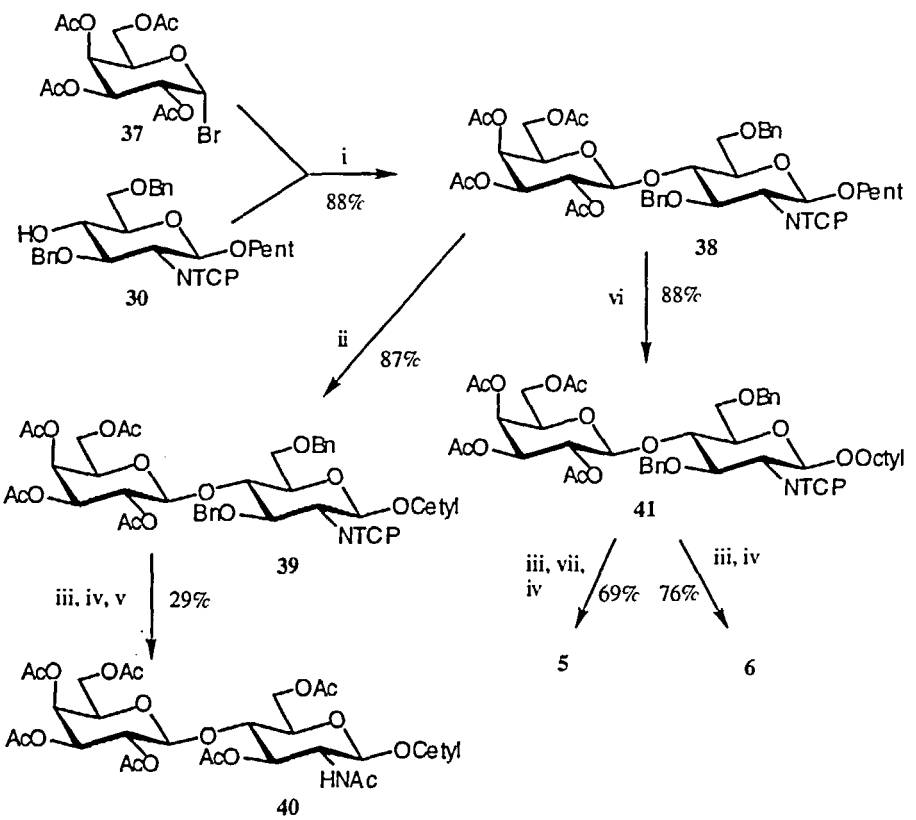
Scheme 5 **i**: $CH_3(CH_2)_{14}CH_2OH$, DMTST, CH_2Cl_2 ; **ii**: H_2/Pd; **iii**: 1M NaOMe, MeOH; **iv**: 1M NaOH

Some cleavage of the reducing end glucosamine could be noted during these conditions but not to an unacceptable extent. Hydrogenolysis reduced the azide function and removed the benzyl groups and the first target **2** was produced in 38% yield from fully protected **35** after final purification. Selective *N*-acetylation of **2** with acetic anhydride in methanol produced the next target trisaccharide **1** (31% from 27).

Similar pathways were performed to produce the disaccharide targets **3** and **4**. Disaccharide building block **13** was activated by DMTST in the presence of cetyl alcohol. These conditions gave alkyl disaccharide **36** in 90% yield (Scheme 5). Reduction of the azide by hydrogenolysis followed by standard removal of the acetyl and benzoyl groups with sodium methoxide gave the *N*-acetyl compound **3** in 46% over two steps. No *N*-acetylation was necessary due to acyl migration to the amino group during deacetylation. Further basic treatment of disaccharide **3** with aqueous sodium hydroxide removed the *N*-acetyl and the aminodisaccharide **4** was produced (41% yield from **36**).

The remaining disaccharide units, **5** and **6**, corresponding to lactosamine, were synthesised from building block **30** and 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide (**37**) (Scheme 6). Silver triflate promoted coupling produced the protected *n*-pentenyl disaccharide **38** in 88%. Activation of the *n*-pentenyl with NIS and TESOTf in the presence of cetyl alcohol then gave the complete aglycon linked lactosamine **39** in 87% yield. Prolonged treatment of **39** with ethylenediamine removed the TCP group along with the acetyl groups. Hydrogenolysis finalised the deprotection with cleavage of the remaining benzyl groups.

However, purification and characterisation of the fully deprotected residue turned out to be difficult. Solubility was poor in a wide variety of solvents resulting in difficult purification and unsatisfactory NMR experiments. To prove that the correct compound was formed in the deprotection procedure, the product was acetylated using standard conditions



Scheme 6 i: AgOTf, *sym*-collidine, CH_2Cl_2, -30 °C; **ii**: $CH_3(CH_2)_{14}CH_2OH$, NIS, TESOTf, CH_2Cl_2; **iii**: ethylenediamine, CH_3CN:EtOH:THF 2:1:1, 60 °C; **iv**: H_2/Pd; **v**: Ac_2O, pyridine; **vi**: $CH_3(CH_2)_6CH_2OH$, NIS, TESOTf, CH_2Cl_2; **vii**: Ac_2O, MeOH

and indeed the peracetylated lactosamine **40** was readily isolated (Scheme 6). Use of a shorter alkyl chain, octyl, as aglycon in place of cetyl would hopefully simplify the purification and still provide acceptable micelle forming capability. Therefore *n*-octanol was coupled to the disaccharide donor **38** to produce octyl glycoside **41** in 88% yield (Scheme 6). The TCP and acetyl groups were removed with ethylenediamine overnight. Selective *N*-acetylation followed by hydrogenolysis then produced the target compound **5** in 69% from **41**. The same procedure, but omitting the *N*-acetylation, gave the free lactosamine glycoside **6** as the last target in 76%.

In general, deprotection and purification of the final products were difficult and tedious due to the amphiphilic character of the produced compounds. Low solubility and

often poor performance in standard purification procedures gave lower yields than desired. These problems were most pronounced during deprotection of lactosamine derivative **39**. To obtain satisfactory degree of characterisation and purity, the cetyl alcohol had to be abandoned in favour of the significantly shorter octyl. Similar problems have been reported by others during work with long lipophilic alkyl chains or spacers.[46-48] Nonetheless, the overall strategy described here allows a number of different di- and trisaccharides to be synthesised from a few building blocks. Yields in both the protecting group chemistry and the glycosylation reactions are appealing. Further variation at the reducing end with other spacers and manipulation of the amino functions can be done depending on the outcome of the biological experiments and examination of the compounds micelle forming capability now in progress.

EXPERIMENTAL

General Methods. Organic solutions were dried over $MgSO_4$ before concentrations, which were performed under reduced pressure at ≤40 °C (waterbath). TLC was performed on silica gel 60 F_{254} (Merck) with detection by UVlight and/or charring with 8% sulfuric acid or AMC (ammonium molybdate 10g, cerium(IV) sulfate 2 g, dissolved in aq 10% H_2SO_4 2 L). Silica Gel (0.0404-0.063 mm, Amicon) was used for column chromatography. Size exclusion chromatography was performed on Sephadex® LH-20. NMR spectra were recorded in $CDCl_3$ at 25 °C (internal standard Me_4Si, δ=0.00) unless otherwise stated, using a JEOL GX-270 instrument at 270 MHz (^1H) or 67.5 MHz (^{13}C) or a Varian Mercury 300 at 300 MHz (^1H) or 75 MHz (^{13}C). Heteronuclear single quantum coherence (HSQC) experiment for compound **32** was recorded on a Varian inova 400 instrument. ^1H NMR and phase-sensitive ^1H-^1H correlation spectra (^1H-^1H COSY) for compound **34** were recorded on a Varian inova 600 instrument. Melting points are corrected. Optical rotations were recorded at room temperature with a Perkin-Elmer 241 polarimeter using a 10 cm 1 mL cell. High Resolution Fast Atom Bombardment Mass Spectrometry (HRMS) was performed in the positive ion mode at a resolution of 10k on a JEOL JMS-SX 102A mass spectrometer using 3-nitrobenzyl alcohol as a matrix.

Ethyl 2,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-1-thio-β-D-galacto-pyranoside (8) and Ethyl 2,3-di-*O*-benzoyl-4,6-*O*-isopropylidene-1-thio-β-D-galactopyranoside (9). Tetraol **7**[9,10] (7.98 g, 35.6 mmol) was stirred with acetone (270 mL) and *p*TsOH (270 mg, 1.4 mmol) at room temperature for 2 h. The mixture was neutralised with pyridine and concentrated. The remaining residue was dissolved in pyridine (170 mL) and benzoyl chloride (13.0 mL, 124.6 mmol) was added to the

solution. After stirring at room temperature for 3 h the mixture was concentrated, dissolved in CH_2Cl_2, and washed with 1M HCl, sat aq $NaHCO_3$ and H_2O. The organic phase was then dried, concentrated and co-concentrated twice with toluene. Flash chromatography (toluene-EtOAc 20:1) gave **8** (12.75 g, 27.0 mmol, 76%). Recrystallization from EtOAc-light petroleum gave white crystals having mp 144-145 °C, $[\alpha]_D$ +65,8° (*c* 1.0, $CHCl_3$). NMR data ($CDCl_3$): ^{13}C, δ 15.0 (SCH_2CH_3), 24.5 (SCH_2CH_3), 26.3, 27.7 (CH_3 isoprop), 63.9, 72.2, 73.8, 74.4, 77.2 (C-2-C-6), 83.0 (C-1), 110.9 (isoprop C), 128.3-133.2 (aromatic C), 165.4, 166.3 (C=O benzoyl); ^1H δ 1.21 (*t*, 3H, SCH_2CH_3), 1.35, 1.61 (s, 6H, CH_3 isoprop.), 2.68 (m, 2H, SCH_2CH_3), 4.16-4.24 (m, 1H, H-5), 4.32-4.40 (m, 2H, H-4, H-6), 4.54-4.4.70 (m, 3H, H-1, $J_{1,2}$ 9.89 Hz, H-3, H-6), 5.28 (dd, 1H, H-2), 7.24-8.05 (m, 10H, aromatic H).

Anal. Calcd for $C_{25}H_{28}O_7S$: C, 63.54; H, 5.97; S, 6.78%. Found: C, 63.59; H, 6.06; S, 6.86%.

Compound **9** was also isolated as a minor product (2.52 g, 5.3 mmol, 15%). NMR data ($CDCl_3$): ^{13}C, δ 14.8 (SCH_2CH_3), 18.6 (CH_3 isoprop), 23.0 (SCH_2CH_3), 29.1 (CH_3 isoprop), 62.8, 66.9, 67.3, 69.9, 74.0 (C-2-C-6), 82.7(C-1), 99.0 (isoprop C), 128.3-133.3 (aromatic C), 165.4, 166.1 (C=O benzoyl); ^1H δ 1.3 (t, 3H, SCH_2CH_3), 1.37, 1.47 (s, 6H, CH_3 isoprop), 2.74-2.96 (m, 2H, SCH_2CH_3), 3.58 (m, 1H, H-5), 4.05 (m, 2H, H-6), 4.58 (d, 1H, H-4), 4.66 (d, 1H, H-1, $J_{1,2}$ 9.89 Hz), 5.28 (dd, 1H, H-3), 5.91 (dd, 1H, H-2), 7.15-7.99 (m, 10H, aromatic H).

Ethyl 2,6-di-*O*-benzoyl-1-thio-β-D-galactopyranoside (10). A solution of **8** (11.92 g, 25.25 mmol) in aq TFA (90%, 20 mL) was stirred at room temperature for 15 min. The mixture was diluted with toluene and concentrated. Flash chromatography (toluene-EtOAc 2:1) of the residue gave **10** (8.73 g, 20.2 mmol, 80%). Recrystallization (EtOAc-light petroleum) gave crystals having mp 147-148 °C, $[\alpha]_D$ +2.6° (*c* 1.0, $CHCl_3$). NMR data ($CDCl_3$): ^{13}C, δ 15.0 (SCH_2CH_3), 24.2 (SCH_2CH_3), 63.3, 69.0, 72.1, 73.5, 76.2 (C-2-C-6), 83.5 (C-1), 128.4-133.3 (aromatic C), 166.6, 166.8 (C=O benzoyl); ^1H δ 1.21 (t, 3H, SCH_2CH_3), 2.68 (m, 2H, SCH_2CH_3), 3.84-3.92 (m, 2H, H-3, H-5), 4.10 (d, 1H, H-4), 5.53-4.69 (m, 3H, H-1 J1, 2 9.89 Hz, H-6), 5.33 (t, 1H, H-2), 7.29-8.15 (m, 10H, aromatic H).

Anal. Calcd for $C_{22}H_{24}O_7S$: C, 61.10; H, 5.59; S, 7.41%. Found: C, 61.27; H, 5.73; S, 7.38%.

Ethyl 2,3,6-tri-*O*-benzoyl-1-thio-β-D-galactopyranoside (11). Dibutyl tinoxide (105 mg, 0.42 mmol) was added to a solution of **10** (182 mg, 0.42 mmol) in MeOH (10 mL). The mixture was refluxed under argon for 2.5 h and then concentrated and dried under vacuum. The residue was dissolved in THF (8 mL) and triethylamine (64 μL, 0.46 mmol) and benzoyl chloride (53 μL, 0.46 mmol) were added. The mixture was

stirred at room temperature under argon for 3 h and then concentrated. Flash chromatography (toluene-EtOAc 6:1) gave **11** (194 mg, 0.36 mmol, 86%) which was recrystallized from EtOAc-light petroleum to give white crystals having mp 114 °C, $[\alpha]_D$ +53.7° (*c* 1.0, $CHCl_3$). NMR data ($CDCl_3$): ^{13}C, δ 14.9 (SCH_2CH_3), 24.2 (SCH_2CH_3), 63.4, 67.5, 68.1, 75.3, 76.2 (C-2-C-6), 83.8 (C-1), 128.2-133.3 (aromatic C), 165.5, 165.9, 166.5 (C=O, benzoyl); ^1H δ 1.23 (t, 3H, $SCH2CH_3$), 2.76 (m, 2H, SCH_2CH_3), 3.33 (broad signal, 1H, OH-4), 4.12 (t, 1H, H-5), 4.45 (d, 1H, H-4) 4.65 (m, 2H, H-6), 4.79 (d, 1H, H-1, $J_{1,2}$ 9.89 Hz), 5,45 (dd, 1H, H-3), 5.92 (t, 1H, H-2), 7.10-8.07 (m, 15H, aromatic H).

An analytical amount of **11** was acetylated (Ac_2O/pyridine 2:3) and purified. ^1H NMR signal with characteristic coupling constant corresponding to H-4, was shifted downfield.

Anal. Calcd for $C_{29}H_{28}O_8S$: C, 64.91; H, 5.26; S, 5.98%. Found: C, 65.12; H, 5.39; S, 5.87%.

Ethyl (3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-(1→4)-2,3,6-tri-*O*-benzoyl-1-thio-β-D-galactopyranoside (13). A solution of 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl bromide **12**[18] (788 mg, 2.0 mmol), **11** (1.18 g, 2.2 mmol), and *sym*-collidine (237 μL, 1.8 mmol) in CH_2Cl_2 (20 mL) was stirred with powdered 4Å molecular sieves for 20 min at –35 °C, before silver triflate (AgOTf) (1.03 g, 4.0 mmol) was added. After 2 h the reaction was quenched with triethylamine (2 mL), and after stirring for 15 min the mixture was diluted with CH_2Cl_2, filtered through Celite and concentrated. Chromatography (light petroleum-EtOAc 2:1) of the residue gave **13** (1.42 g, 1.67 mmol, 86%) as a white foam, $[\alpha]_D$ +92° (*c* 1.0, $CHCl_3$). NMR data ($CDCl_3$): ^{13}C, δ 14.9 (SCH_2CH_3), 20.5, 20.6 (2 signals) (CH_3 acetyl), 24.0 (SCH_2CH_3), 61.1, 62.0, 62,3, 67.8, 67.9, 68.6, 71.1, 74.6, 76.0, 76.1 (C-2-C-6, C-2'-C-6'), 84.0 ($J_{C-1, H-1}$ 154 Hz, C-1), 98.9 ($J_{C-1, H-1}$ 172 Hz, C-1'), 128.4-133.8 (aromatic C), 165.3, 165.9, 166.0 (C=O benzoyl), 169.6, 169.8, 170.4 (C=O acetyl); ^1H, δ 1.26 (t, 3H, SCH_2CH_3), 1.93, 2.03, 2.08 (s, 9H, CH_3 acetyl), 2.79 (m, 2H, SCH_2CH_3), 3.50 (dd, 1H, H-2'), 3.64 (dd, 1H, H-6'), 7.86 (dd, 1H, H-6'), 4.16 (m, 1H, H-5), 4.35 (m, 1H, H-5'), 4.51 (d, 1H, H-4), 4.74 (m, 2H, H-6), 4.77 (d, 1H, H-1, $J_{1,2}$ 9.89 Hz), 5.02-5.06 (m, 2H, H-1', $J_{1,2}$ 3.66 Hz, H-4'), 5.40 (dd, 1H, H-3), 5.54 (t, 1H, H-3'), 5.78 (t, 1H, H-2), 7.25-8.05 (m, 15H, aromatic H).

Anal. Calcd for $C_{41}H_{43}O_{15}N_3S$: C, 57.94; H, 5.10; N, 4.94%. Found: C, 57.85; H, 5.13; N, 4.98%.

Hexadecyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside (15). $Hg(CN)_2$ (2.07 g, 8.20 mmol) and $HgBr_2$ (2.96 g, 8.20 mmol) were added to a stirred solution of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucosyl chloride (**14**)[20] (3.0 g, 8.20 mmol), cetyl alcohol (3.73 g, 14.8 mmol) and Drierite in dry toluene

(30 mL). After stirring for 24 h the mixture was diluted with CH_2Cl_2, filtered through Celite and concentrated. The residue was dissolved in CH_2Cl_2 and washed with aq 30% KI, sat aq $NaHCO_3$ and H_2O. The organic layer was dried, filtered and concentrated. Column chromatography (toluene-EtOAc 1:1) afforded **15** (3.05 g, 5.33 mmol, 65%) as a white solid. $[\alpha]_D$ -10.0°(*c* 0.5, $CHCl_3$). NMR data ($CDCl_3$): ^{13}C, δ 14.1 (CH_3 alkyl chain), 20.6 (3 signals, CH_3 acetyl), 22.6 (CH_3 acetyl), 23.2-31.9 (alkyl chain C), 54.8, 62.2, 68.7, 69.9, 71.7, 72.4 (C-2-C-6), 100.6 (C-1, $J_{C-1,\ H-1}$ 166 Hz), 169.4, 170.1, 170.7, 170.8 (C=O acetyl), ^1H, δ 0.84 (t, 3H, CH_3 alkyl chain), 1.20-1.52 (m, 28H, alkyl chain H), 1.90, 1.98, 1.99, 2.03 (s, 12H, CH_3 acetyl), 3.39-3.50 (m, 1H, OCH_2 alkyl chain), 3.75-3.92 (m, 3H, H-5, H-2, O-CH_2 alkyl chain), 4.09 (dd, 1H, H-6), 4.23 (dd, 1H, H-6), 4.66 (d, 1H, H-1 $J_{1,2}$ 8.51 Hz), 5.02 (dd, 1H, H-4), 5.28 (dd, 1H, H-3), 5.90 (d, 1H, HNAc).

Anal. Calcd for $C_{30}H_{53}O_8N$: C, 63.02; H, 9.34; N, 2.45%. Found: C, 63.41; H, 9.51; N, 2.39%.

Hexadecyl 2-acetamido-3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (16). Derivative **15** (2.27 g, 3.97 mmol) was dissolved in MeOH (50 mL) and treated with a catalytic amount of 1M NaOMe in MeOH. After stirring for 15 min the mixture was concentrated and dried in vacuo. To a mixture of the residue and α,α–dimethoxytoluene (25 mL) in DMF (25 mL) was added *p*-toluenesulfonic acid (250 mg). The mixture was stirred for 2 h at 50 °C and then neutralised with triethylamine. The product was crystallised from the reaction mixture by adding *n*-hexane (200 mL) under vigorous stirring. The crystals were filtered, washed with ice-cold *n*-hexane and then dissolved in pyridine (30 mL) and treated with Ac_2O (20 mL). After 30 min the reaction mixture was concentrated and co-concentrated twice with toluene. The residue was subjected to column chromatography ($CHCl_3$-MeOH 5:1) to yield **16** (1.51 g, 2.62 mmol, 66%). $[\alpha]_D$ -19.7°(*c* 0.7, $CHCl_3$). NMR data ($CDCl_3$): 13C, δ 14.2 (CH_3 alkyl chain), 21.1, 22.8 (CH_3 acetyl), 23.3-32.0 (alkyl chain C), 54.6, 66.3, 68.8, 70.2, 72.2, 78.9 (C-2-C-6, OCH_2 alkyl chain), 101.4 (C-1), 102.1 (C benzylidene), 126.2-137.1 (aromatic C), 170.3, 171.5 (C=O acetyl); ^1H δ 0.88 (t, 3H, CH_3 alkyl chain), 1.0-1.51 (m, 28H, alkyl chain H), 1.96, 2.08 (s, 6H, CH_3 acetyl), 3.11-3.15 (m, 1H, OCH_2 alkyl chain), 3.30-3.38 (m, 1H, H-5), 3.52-3.57 (m, 1H, H-4), 3.66-3.82 (m, 2H, H-6, OCH_2 alkyl chain), 4.09 (dd, 2H, H-2), 4.31 (dd, 1H, H-6), 4.47 (d, 1H, H-1 $J_{1,2}$ 8.42Hz), 5.28 (dd, 1H, H-3), 5.50 (s, 1H, acetal H), 6.00 (d, 1H, HNAc), 7.26-7.43 (m, 5H, aromatic H).

Anal. Calcd for $C_{33}H_{53}O_7N$: C, 68.84; H, 9.28; N, 2.43%. Found: C, 69.00; H, 9.38; N, 2.28%.

Hexadecyl 2-acetamido-3-*O*-acetyl-6-*O*-benzyl-2-deoxy-β-D-glucopyranoside (17). To a mixture of **16** (2.18 g, 3.79 mmol), $NaBH_3CN$ (2.17g, 34.5

mmol) and powdered 3Å molecular sieves in dry THF was added HCl/ether solution until the evolution of gas ceased. The reaction mixture was stirred for 2 h, diluted with THF, filtered through Celite and concentrated. Flash chromatography (toluene-EtOAc 1:3) of the residue afforded **17** (1.62 g, 2.80 mmol, 74%) as a solid. $[\alpha]_D$ -31.0°(*c* 0.8, $CHCl_3$). NMR data ($CDCl_3$): ^{13}C, δ 14.2 (CH_3 alkyl chain), 21.1, 22.7 (CH_3, acetyl), 23.3-32.0 (alkyl chain C), 54.3, 69.8, 70.5, 70.9, 73.8, 74.1, 75.6 (C-2-C-6, CH_2 benzyl), 101.0 (C-1), 170.5, 172.1 (C=O acetyl); ^1H, δ 0.88 (t, 3H, CH_3 alkyl chain), 1.24-1.53 (m, 28H, alkyl chain), 1.93, 2.09 (s, 6H, CH_3 acetyl), 3.17 (broad signal, 1H, 4-OH), 3.36-3.49 (m, 1H, OCH_2 alkyl chain), 3.51-3.58 (m, 1H, H-5), 3.67-3.94 (m, 5H, H-2, H-4, H-6, OCH_2-alkyl chain), 4.50 (d, 1H, H-1, $J_{1,2}$ 8.43 Hz), 4.58 (dd, 2H, CH_2 benzyl), 5.06 (dd, 1H, H-3), 5.88 (d, 1H, HNAc).

Anal calcd for $C_{33}H_{55}O_7N$: C, 68.60; H, 9.60; N, 2.42%. Found: C, 68.44; H, 9.76; N,2.57%.

Hexadecyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside (21). TESOTf (713 μL, 3.15 mmol) was added to a stirred solution of pent-4-enyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-tetrachlorophthalimido-2-deoxy-β-D-glucopyranoside (**20**)[30] (1.99g, 2.87 mmol), cetyl alcohol (1.39 g, 5.73 mmol) and NIS (742 mg, 3.29 mmol) in CH_2Cl_2 (20 mL). After 10 min, the reaction mixture was diluted with CH_2Cl_2, washed with sat aq $Na_2S_2O_3$ and sat aq $NaHCO_3$. The organic phase was then dried and concentrated. Column chromatography of the residue (light petroleum- EtOAc 6:1) gave **21** (1.66 g, 1.95 mmol, 68%) as a foam. $[\alpha]_D$ +52.0°(*c* 0.9 $CHCl_3$). NMR data ($CDCl_3$): ^{13}C, δ 14.0 (CH_3 alkyl chain), 22.5-31.8 (alkyl chain C), 56.4, 68.5, 68.7, 75.1, 76.5, 78.3, 82.6 (C-2-C6, OCH_2 alkyl chain), 98.3 (C-1, $J_{C-1,\ H-1}$ 169.4 Hz), 101.2 (benzylidene C), 125.9-139.6 (aromatic C), 163.1, 163.2 (C=O, TCP); ^1H, δ 0.88 (t, 3H, CH_3 alkyl chain), 1.0-2.51 (m, 28H, alkyl chain), 3.34 (m, 1H, OCH_2 alkyl chain), 3.57-3.63 (m, 1H, H-5), 3.72-3.89 (m, 3H, OCH_2 alkyl chain, H-4, H-6), 4.14 (dd, 1H, H-2), 4.29-4-42 (m, 3H, H-3, H-6, CH_2 benzyl), 4.82 (d, 1H, CH_2 benzyl), 5.17 (d, 1H, H-1, $J_{1,2}$ 8.52 Hz), 5.63 (s, 1H, acetal H), 6.70-7.73 (m, 10H, aromatic H).

Anal. Calcd for $C_{44}H_{53}O_7Cl_4N$: C, 62.19; H, 6.28; N, 1.65%. Found: C, 62.16; H, 6.42; N, 1.63%.

Hexadecyl 3,6-di-*O*-benzyl-2-tetrachlorophthalimido-2-deoxy-β-D-glucopyranoside (22). A solution of **21** (1.11 g, 1.31 mmol) and $NaBH_3CN$ (823 mg, 13.1 mmol) in dry THF (15 mL) containing powdered 3Å molecular sieves was stirred for 30 min before a solution of HCl/Et_2O was added until the evolution of gas ceased. After stirring in room temperature for 20 min the mixture was diluted with THF, filtered through Celite and concentrated. Flash chromatography of the residue yielded **22**

(781 mg, 0.917 mmol, 70%) as an oil. $[\alpha]_D$ +36.3°(*c* 0.9, $CHCl_3$). NMR data ($CDCl_3$): ^{13}C, δ 14.2 (CH_3 alkyl chain), 22.8-32.0 (alkyl chain C), 56.1, 69.6, 70.7, 73.4, 73.8, 74.8, 74.9, 79.4 (C-2-C-6, OCH_2 alkyl chain), 97.8 (C-1), 126.6-139.4 (aromatic C), 162.3, 163.1 (C=O, TCP); ^1H, δ 0.88 (t, 3H, CH_3), 1.05-2.51 (m, 28H, alkyl chain), 3.03 (broad signal, 1H, 4-OH), 3.30-3.40 (m, 1H, OCH_2 alkyl chain), 3.57-3.63 (m, 1H, H-5), 3.69-3.87 (m, 4H, OCH_2 alkyl chain, H-6, H-4), 4.43 (d, 1H, CH_2 benzyl), 4.62 (dd, 2H, CH_2 benzyl), 4.85 (d, 1H, CH_2 benzyl), 5.08 (d, 1H, H-1, $J_{1,2}$ 7.97 Hz) 6.74-7.37 (m, 10H, aromatic H).

Anal. Calcd for $C_{44}H_{55}O_7Cl_4N$: C, 62.05; H, 6.51; N, 1.64%. Found: C, 62.06; H, 6.40; N, 1.63%.

Hexadecyl 2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (23). A solution of **22** (0.5 g, 0.587 mmol) and ethylenediamine (1.5 mL) in EtOH:THF 1:1 (20 mL) was kept at 70 °C for 15 h. The mixture was then concentrated and co-concentrated twice with toluene. The residue was dissolved in pyridine (9 mL) and Ac_2O (6 mL) and the mixture was stirred at room temperature for 3 h. concentrated and co-concentrated with toluene. The residue was purified on a short silica gel column (light petroleum-EtOAc). The obtained material was dissolved in MeOH:CH_2Cl_2 (10 mL) and treated with a catalytic amount of 1M NaOMe in MeOH solution. After stirring in room temperature for 3 h the reaction was neutralised with Dowex 50 H^+, filtered and concentrated. After flash chromatography (light petroleum-EtOAc 2:1) **23** (320 mg, 0.511 mmol, 87%) was obtained. $[\alpha]_D$ -53.8°(*c* 0.8, $CHCl_3$). NMR data ($CDCl_3$): ^{13}C, δ 14.0 (CH_3 alkyl chain), 22.6 (CH_3, acetyl), 22.7-31.8 (alkyl chain C), 59.7, 69.6, 70.6, 73.1, 73.6, 73.8, 74.0, 80.3 (C-2-C-6, OCH_2 alkyl chain), 99.8 (C-1), 127.6-138.5 (aromatic C), 170.4 (C=O acetyl); 1H, δ 0.88 (t, 3H, CH_3 alkyl chain), 1.24-1.55 (m, 28H, alkyl chain H), 1.89 (s, 3H, CH_3 acetyl), 3.24 (m, 1H, H-2), 3.40-3.48 (m, 1H, CH_2, alkyl chain), 3.51-3.56 (m, 1H, H-5), 3.64 (dd, 1H, H-4), 3.74-3.83 (m, 3H, H-6, OCH_2 alkyl chain), 4.05 (dd, 1H, H-3), 4.58 (dd, 2H, CH_2 benzyl), 4.55 (d, 1H, CH_2 benzyl), 4.61 (d, 1H, CH_2 benzyl), 4.87 (d, 1H, H-1, $J_{1,2}$ 8.24 Hz), 5.60 (d, 1H, HNAc), 7.26-7.35 (m, 10H, aromatic H).

Anal. Calcd for $C_{38}H_{59}O_6N$: C, 72.92; H, 9.50; N, 2.24%. Found: C, 72.66; H, 9.51; N, 2.19%.

Pent-4-enyl 6-*O*-benzyl-2-tetrachlorophthalimido-2-deoxy-β-D-glucopyranoside (24). To a solution of pent-4-enyl 4,6-*O*-benzylidene-2-tetrachlorophthalimido-2-deoxy-β-D-glucopyranoside (**19**)[30] (997 mg, 1.65 mmol) and $NaBH_3CN$ (1.03 g, 16.5 mmol) in dry THF (20 mL) containing 3Å molecular sieves, was added HCl/ether solution until the evolution of gas ceased. The reaction was stirred for 1h, diluted with THF, filtered through Celite and concentrated. Flash chromatography

(toluene-EtOAc 4:1) of the residue gave the diol **24** (908 mg, 1.50 mmol, 91%) as a foam. $[\alpha]_D$ -29.0° (*c* 0.2, $CHCl_3$). NMR data ($CDCl_3$): ^{13}C, δ 28.7, 30.1 (CH_2 pentenyl), 57.6, 69.0, 69.8, 71.4, 71.9, 73.7, 75.8 (C-2-C-H6, OCH_2 pentenyl, CH_2 benzyl), 98.1 (C-1), 114.7 (CH_2= pentenyl), 125.2-140.0 (aromatic C, CH= pentenyl), 162.2, 163.1 (C=O TCP); ^1H, δ 1.45-1.56 (m, 2H, CH_2 *pentenyl*), 1.80-1.92 (m, 2H, CH_2 *pentenyl*), 3.38-3.45 (m, 1H, OCH_2 pentenyl), 3.57-3.64 (m, 2H, H-4, H-5), 3.85 (m, 3H, H-6, OCH_2 pentenyl), 4.12 (dd, 1H, H-2), 4.27 (dd, 1H, H-3), 4.60 (dd, 2H, CH_2 benzyl), 4.80-4.87 (m, 2H, CH_2= pentenyl), 5.15 (d, 1H, H-1 $J_{1,2}$ 8.24 Hz), 5.60-5.70 (m, 1H, CH= pentenyl), 7.26-7.37 (m, 5H, aromatic H).

Anal. Calcd for $C_{26}H_{25}O_7Cl_4N$: C, 51.59; H, 4.16; N, 2.31%. Found: C, 51.46; H, 4.07; N, 2.21%.

Ethyl 3-*O*-acetyl-6-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (26). Ethyl 3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**25**) (2.06 g, 4.41 mmol) and $NaBH_3CN$ (2.77 g, 44.1 mmol) were reacted and worked up as described for **24**. Chromatography (toluene-EtOAc 1:1) of the residue gave compound **26** (1.72g, 3.66 mmol, 83%) as a white foam. $[\alpha]_D$ –2.73°(c 0.11, $CHCl_3$). NMR data ($CDCl_3$): ^{13}C, δ 15.0 (SCH_2CH_3), 20.7 (CH_3 acetyl), 24.3 (SCH_2CH_3), 53.7, 70.3, 71.1, 73.7, 74.3, 78.5 (C-2-C-6, CH_2 benzyl), 80.9 (C-1), 123.6-137.8 (aromatic C), 167.4, 167.8 (C=O NPhth), 171.2 (C=O acetyl), ^1H, δ 1.22 (t, 3H, SCH_2CH_3), 1.90 (s, 3H, CH_3 acetyl), 2.60-2.73 (m, 2H SCH_2CH_3), 3.78-3.83 (m, 4H, H-3, H-4, H-5, H-6), 4.31 (dd, 1H, H-2), 4.61 (dd, 2H, CH_2 benzyl), 5.56 (d, 1H, H-1, $J_{1,2}$ 10.26 Hz), 5.74 (dd, 1H, H-3), 7.14-7.85 (m, 10H, aromatic H).

Anal. Calcd for $C_{25}H_{27}O_7NS$: C, 61.84; H, 5.61; N, 2.88%. Found: C, 61.74; H, 5.48%.

General procedure for the silver triflate couplings. Thioglycoside **13** was transformed into the corresponding bromosugar **18** as described for **31**. A mixture of the bromosugar (1 eq), the acceptor (1.1 eq) and powdered 4Å molecular sieves in CH_2Cl_2 was stirred for 20 min at –30 °C before AgOTf (2 eq) was added. After 2 h triethylamine (1mL) was added and, the reaction was allowed to attain room temperature before it was diluted with CH_2Cl_2, filtered through Celite and concentrated.

Pent-4-enyl (3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside (31). Thioglucoside **13** (886 mg, 1.02 mmol) was dissolved in CH_2Cl_2 (15 mL) and bromine (419 μL, 8.16 mmol) was added. The mixture was stirred under argon in room temperature for 2 h and then concentrated, co-concentrated with toluene (Na-dried) and dried under vacuum. NMR ($CDCl_3$) showed characteristic shifts for the anomeric carbon

(δ 88.9) and proton (δ 6.84, $J_{1,2}$ 4.0 Hz). A solution of the residue, pent-4-enyl 3,6-di-*O*-benzyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside (**30**) (924 mg, 1.33 mmol) and *sym*-collidine (94 μL, 0.71 mmol) in CH_2Cl_2, (20 mL) was stirred with powdered 4Å molecular sieves for 20 min at –30 °C before AgOTf (524 mg, 2.04 mmol) was added. After 3 h triethylamine (1 mL) was added and the mixture was then allowed to attain room temperature where after it was filtered through Celite and concentrated. Flash chromatography of the residue (light petroleum-EtOAc 3:1-2:1) gave **31** (1.27 g, 0.86 mmol, 84%) as a foam. $[\alpha]_D$ +83.3°(*c* 1.0, $CHCl_3$). NMR data ($CDCl_3$): ^{13}C, δ 20.4, 20.5, 20.7 (CH_3 acetyl), 28.4, 29.8 (CH_2 pentenyl), 56.4, 61.0, 61.8, 61.9, 67.4, 67.8, 68.4, 68.7, 70.1, 70.8, 72.2, 73.2, 73.5, 74.5, 74.7, 75.4, 77.6, 78.4 (C-2-C-6, C-2'-C-6', C-2''-C-6'', CH_2 benzyl, OCH_2 pentenyl), 97.8 (C-1, $J_{C-1,H-1}$ 163.1 Hz), 98.5 (C-1'', $J_{C-1,H-1}$ 172.3 Hz), 100.7 (C-1', $J_{C-1,H-1}$ 164.9 Hz), 114.7 (CH_2= pentenyl), 125.3-139.4 (aromatic C, CH= pentenyl), 163.1, 162.4 (C=O, TCP), 165.0, 165.7, 166.0 (C=O benzoyl), 169.3, 169.7, 170.3 (C=O acetyl).

Anal. Calcd for $C_{72}H_{68}O_{22}N_4Cl_4$: C, 58.31; H, 4.62; N, 3.58%. Found: C, 58.54; H, 4.63; N, 3.76%.

Ethyl (3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-(1→4)-(2,3,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (32). Thioglycoside **13** (184 mg, 0.216 mmol) was treated with Br_2 (89 μL, 1.73 mmol) as described for **31** and the bromosugar formed was reacted with ethyl 3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside **27**[29] (127 mg, 0.238 mmol) and AgOTf (111 mg, 0.432 mmol) according to the general procedure. Flash chromatography (light petroleum-EtOAc 3:1-2:1) of the crude product afforded **32** (162 mg, 0.123 mmol, 57%). $[\alpha]_D$ +86.0° (*c* 0.2, $CHCl_3$) NMR data ($CDCl_3$): ^{13}C, δ 14.1 (SCH_2CH_3), 20.3 (3 signals, CH_3 acetyl), 23.7 (SCH_2CH_3), 54.7, 60.3, 61.0, 61.6, 67.6, 67.8, 68.3, 70.1, 70.9, 72.1, 73.2, 73.4, 74.7 (2 signals), 77.3, 78.1, 78.7(C-2-C-6, C-2'-C-6', C-2''-C-6'', CH_2 benzyl), 80.9 (C-1 $J_{C-1,H-1}$ 157.5 Hz), 98.4 (C-1'' $J_{C-1,H-1}$ 175.1 Hz), 100.5 (C-1' $J_{C-1,H-1}$ 168.6 Hz), 123.1-138.6 (aromatic C), 164.9, 165.7, 165.8 (C=O benzoyl), 167.6 (C=O NPhth), 169.2, 169.6, 170.2 (C=O acetyl), ^1H, δ 1.12 (t, 3H, SCH_2CH_3), 1.76, 1.93 (2 signals) (s, 9H, CH_3, acetyl), 2.49-2.66 (m, 2H, SCH_2CH_3), 3.41-3.60 (m, 5H, H-6'', H-2'', H-5, H-6), 3.70-3.79 (dd, 1H, H-6''), 3.81-3.91 (m, 2H, H-4, H-3), 4.15-4.41 (6H, H-5', H-5'', H-2, H-4', CH_2 benzyl), 4.60-4.73 (m, 3H, H-6', CH_2 benzyl), 4.89-5.02 (m, 4H, H-1', H-4'', H-6', H-1'), 5.14 (d, 1H, H-1, $J_{1,2}$ 10.16 Hz), 5.22 (dd, 1H, H-3'), 5.42 (dd, 1H, H-3''), 5.75 (dd, 1H, H-2'), 6.80-8.10 (m, 25H, aromatic H).

Anal. Calcd for $C_{69}H_{68}O_{22}N_4S$: C, 61.97; H, 5.13; N, 4.19%. Found: C, 61.99; H, 5.11; N, 4.03%.

Ethyl (3,4,6-tri-O-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-(1→4)-(2,3,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-6-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (33). Thioglycoside **13** (261 mg, 0.308 mmol) was transformed into the corresponding bromosugar according to the procedure described for **31** and then reacted with ethyl 6-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**28**)[34] (150 mg, 0.339 mmol) and AgOTf (158 mg, 0.616 mmol) as described in the general procedure. The residue was subjected to flash chromatography (toluene-EtOAc 6:1) to yield **33** (257 mg, 0.219, 68%). $[\alpha]_D$ +29.0° (*c* 1.0, $CHCl_3$) NMR data ($CDCl_3$): ^{13}C, δ 15.1 (SCH_2CH_3), 20.8 (3 signals, CH_3 acetyl), 24.0 (SCH_2CH_3), 55.2, 61.2, 62.1, 63.0, 68.0, 68.3, 68.8, 69.4, 70.9, 71.2, 73.1 (2 signals), 73.5, 76.1, 78.0, 81.1 (C-2-C-6, C-2'-C-6', C-2''-C-6'', CH_2 benzyl), 82.5 (C-1), 99.2 (C-1'' $J_{C\text{-}1,\ H\text{-}1}$ 168.0 Hz), 102.0 (C-1' $J_{C\text{-}1,\ H\text{-}1}$ 171.2 Hz) 123.4-138.4 (aromatic C), 165.1, 165.9, 166.3 (C=O benzoyl), 167.8, 168.1 (C=O NPhth), 169.8 (2 signals), 170.5 (C=O acetyl); ^1H, δ 1.18 (t, 3H, SCH_2CH_3), 1.95, 2.04, 2.06 (s, 12H, CH_3 acetyl), 2.47-2.66 (m, 2H, SCH_2CH_3), 3.50-3.65 (m, 5H, H-2'', H-6'', H-6, H-5), 3.80 (dd, 1H, H-4), 3.94 (dd, 1H, H-6''), 4.08 (m,1H, H-5'), 4.16 (d,1H, CH_2 benzyl), 4.27-4.34 (m, 3H, CH_2 benzyl, H-2, H-5''), 4.44 (d, 1H, H-4'), 4.50-4.57 (m, 2H, H-6', H-3), 4.81-4.88 (d, dd, 2H, H-1' $J_{1,2}$ 7.97 Hz, H-6'), 4.95 (d, 1H, H-1'' $J_{1,2}$ 3.85 Hz), 5.01 (dd, 1H, H-4''), 5.26-5.33 (dd, d, 2H, H-3', H-1 $J_{1,2}$ 8.79 Hz), 5.48 (dd, 1H, H-4''), 5.72 (dd, 1H, H-2'), 7.16-8.06 (m, 20H, aromatic H). The anomeric proton (H-1', δ 4.83) showed NOE to protons H-3' (δ 5.30), H-5' (δ 4.08), and H-4 (δ 3.80).

Anal. Calcd for $C_{62}H_{62}O_{22}N_4S$: C, 59.70; H, 5.01; N, 4.49%. Found: C, 59.80; H, 4.72; N, 4.49%.

Pent-4-enyl (3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-gluco-pyranosyl)-(1→4)-(2,3,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-6-*O*-benzyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside (34). Thio-glycoside **13** (191 mg, 0.225 mmol) was treated with Br_2 (92 μL, 1.8 mmol) as described for **31**. The residue was then treated with **24** (150 mg, 0.248 mmol) and AgOTf (116 mg, 0.450 mmol) as described in the general procedure. Flash chromatography (toluene-EtOAc 6:1) gave **34** (245 mg, 0.176 mmol, 78%). $[\alpha]_D$ +72.0° (*c* 0.2, $CHCl_3$) NMR data ($CDCl_3$): ^{13}C, δ 20.7 (3 signals, CH_3 acetyl), 28.5, 29.9 (CH_2 pentenyl), 56.5, 61.1, 62.0, 63.2, 67.9 (2 signals), 68.8 (2 signals), 69.2, 69.5, 71.1, 73.0 (2 signals), 73.4, 73.9, 76.1, 82.6 (C-2-C-6, C-2'-C-6', C-2''-C-6'', CH_2 benzyl, OCH_2 pentenyl), 97.8 (C-1), 99.1 (C-1'', $J_{C\text{-}1,\ H\text{-}1}$ 171.5 Hz), 101.9 (C-1', $J_{C\text{-}1,\ H\text{-}1}$ 165.7 Hz), 114.7 (CH_2= pentenyl), 125.3-140.0 (aromatic C, CH= pentenyl), 162.2, 163.2 (C=O TCP), 165.0, 165.8, 166.3 (C=O benzoyl), 169.7(2C), 170.4 (C=O acetyl); ^1H, δ 1.52-1.59 (m, 2H, CH_2 pentenyl),

1.88-1.96 (m, 2H, CH_2, pentenyl), 1.98, 2.05, 2.07 (s, 9H, CH_3 acetyl), 3.39-3.51 (m, 3H, H-6, OCH_2 pentenyl), 3.56-3.61 (m, 3H, H-2", H-6", H-5), 3.73-3.77 (m, 2H, H-4, OCH_2 pentenyl), 3.96 (dd, 1H, H-6"), 4.10-4.12 (m, 1H, H-5'), 4.14 (d, 1H, CH_2 benzyl), 4.21 (dd, 1H, H-2), 4.27 (d, 1H, CH_2 benzyl), 4.32-4.37 (m, 1H, H-5"), 4.42-4.47 (m, 2H, H-3, H-4'), 4.53-4.56 (m, 1H, H-6'), 4.79 (d, 1H, H-1' $J_{1,2}$ 8.06 Hz), 4.82-4.87 (m, 3H, CH_2= pentenyl, H-6'), 4.95 (d, 1H, H-1", $J_{1,2}$ 3.66 Hz), 5.01-5.04 (dd, 1H, H-4"), 5.14 (d, 1H, H-1, $J_{1,2}$ 8.42 Hz), 5.29 (dd, 1H, H-3'), 5.49 (dd, 1H, H-3"), 5.63-5.67 (m, 1H, CH= pentenyl), 5.17 (dd, 1H, H-2'), 7.15-8.06 (m, 20H, aromatic H). The anomeric proton (H-1', δ 4.79) showed NOE to protons H-3' (δ 5.29), H-5' (δ 4.12), and H-4 (δ 3.73).

Anal. Calcd for $C_{65}H_{62}O_{22}N_4Cl_4$: C, 56.04; H, 4.49; N, 4.02%. Found: C, 55.85; H, 4.48; N, 3.96%.

Hexadecyl (3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-(1→4)-(2,3,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside (35). Method a: Triethylsilyl triflate (TESOTf) (99 μL, 0.438 mmol) was added to a stirred solution of **31** (590 mg, 398 mmol), cetyl alcohol (180 mg, 0.716 mmol) and *N*-iodosuccinimide (NIS) (103 mg, 0.458 mmol) in CH_2Cl_2 (10 mL) at room temperature. After 15 min the mixture was diluted with CH_2Cl_2, washed with sat aq $Na_2S_2O_3$ and sat aq $NaHCO_3$. The organic phase was dried and concentrated. Flash chromatography (light petroleum-EtOAc 3:1) gave **35** (511 mg, 0.310 mmol, 78%) as a foam.

Method b: A solution of **31** (420 mg, 0.283 mmol) and cetyl alcohol (143 mg, 0.567 mmol) in CH_2Cl_2 (10 mL) was stirred with powdered 4Å molecular sieves for 15 min at room temperature before NIS (146 mg, 0.650 mmol) and AgOTf (160 mg, 0.622 mmol) in toluene (Na-dried 3 mL) were added. After 20 min the mixture was diluted with CH_2Cl_2 and filtered through Celite. Work-up and purification as described in method a gave **35** (390 mg, 0.236 mmol, 84%), $[\alpha]_D$ +77.2° (*c* 1.0, $CHCl_3$). NMR data ($CDCl_3$): ^{13}C, δ 14.1 (CH_3 alkyl chain), 20.3, 20.5, 21.5 (CH_3 acetyl), 22.7-31.9 (alkyl chain C), 56.4, 61.0, 61.8 (2 signals), 67.5, 67.8, 68.1, 68.4, 69.5, 70.1, 70.8, 72.2, 73.3, 73.5, 74.5, 74.8, 75.4, 77.6, 78.4 (C-2-C-6, C-2'-C-6', C-2''-C-6'', OCH_2 alkyl chain, CH_2 benzyl), 97.9 (C-1, $J_{C1, H-1}$ 163 Hz), 98.5 (C-1", $J_{C-1, H-1}$ 172 Hz), 100.7 (C-1', $J_{C-1, H-1}$ 163 Hz), 125.3-139.4 (aromatic C), 162.4, 162.5 (C=O TCP), 165.0, 165.8, 166.0 (C=O benzoyl), 169.3, 169.6, 170.3 (C=O acetyl).

Anal. Calcd for $C_{83}H_{92}O_{22}N_4Cl_4$: C, 60.81; H, 5.66; N, 3.42%. Found: C, 60.66; H, 5.51; N, 3.23%.

Hexadecyl (2-amino-2-deoxy-α-D-glucopyranosyl)-(1→4)-β-D-galactopyranosyl-(1→4)-2-amino-2-deoxy-β-D-glucopyranoside (2). A solution

of **35** (660 mg, 0.400 mmol) and ethylenediamine (800 μL, 12 mmol) in CH_3CN:EtOH:THF 2:1:1 (15 mL) was stirred at 60 °C for 4 h. The reaction mixture was then concentrated and co-concentrated three times with toluene. The residue was dissolved in MeOH (15 mL) and NaOMe (catalytic amount of 1M solution in MeOH) was added. The mixture was stirred for 2.5 h, then neutralised with Dowex 50 H^+ resin and concentrated. Flash chromatography ($CHCl_3$-MeOH 20:1+1% triethylamine 10:1+1% triethylamine) gave material (248 mg, 0.265 mmol, 66%) having NMR data (CD_3OD, 25°C, pH 7): ^{13}C, δ 14.3 (CH_3 alkyl chain), 23.7-33.0 (alkyl chain C), 57.5, 61.6, 62.2, 65.4, 69.1, 70.9, 71.9, 72.7, 73.0, 73.5, 74.2 (2 signals), 74.4, 76.4, 76.6, 77.0, 77.5, 78.3, 79.4, 83.7 (C-2-C-6, C-2'-C6', C-2''-C-6'', OCH_2 alkyl chain, CH_2 benzyl), 99.9, 104.0, 104.9 (C-1, C-1', C-1''), 128.7-129.8, 139.6, 139.8 (aromatic C). Further deprotection of this compound was accomplished by hydrogenolysis over Pd/C (10%, 35 mg) in a solution of EtOAc-MeOH-H_2O 2:2:1 (7 mL) in a Parr apparatus (120 psi). After 48 h an additional amount of Pd/C (10%, 25 mg) and acetic acid (0.5 mL) were added to the mixture and hydrogenolysis (120 psi) continued for another 48 h. The mixture was then neutralised with triethylamine, filtered through Celite and concentrated. Purification of the residue on a Sephadex® LH-20 gel column eluted with MeOH gave **2** (116 mg, 0.160 mmol, 40% from **35**) as a glassy solid. $[\alpha]_D$ +24.0°(*c* 0.2, MeOH). NMR data: (CD_3OD, 25°C, pH 7) ^{13}C, δ 14.4 (CH_3 alkyl chain), 23.6-32.9 (alkyl chain C), 56.1, 57.6, 61.4, 61.5, 61.9, 71.1, 71.2, 71.4, 72.2, 72.6, 74.3 (2 signals), 75.8, 76.8, 78.4, 80.5 (C-2-C-6, C-2'-C-6', C-2''-C-6'', OCH_2 alkyl chain), 97.8, 100.3, 105,4 (C-1, C-1', C-1''). HRMS: *m/z* calcd for (M-H)+ 727.4593; Found: 727.4623

Hexadecyl (2-acetamido-2-deoxy-α-D-glucopyranosyl)-(1→4)-β-D-galactopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranoside (1). Ac_2O (47 μL 0.498 mmol) was added to a stirred solution of **2** (60 mg, 0.083 mmol) in MeOH at room temperature. After 3 h the reaction mixture was concentrated and co-concentrated once with toluene. Purification of the residue on a Sephadex® LH-20 gel column eluted with MeOH gave **1** (53 mg, 0.066 mmol, 80%) as a glassy solid. $[\alpha]_D$ +39.0°(*c* 0.2, MeOH). NMR data (CD_3OD, 25°C): ^{13}C, δ 13.7 (CH_3 alkyl chain), 21.9, 22.2 (CH_3 acetyl), 22.9- 32.2 (alkyl chain C), 54.8, 56.3, 60.4, 61.1, 61.5, 69.9, 71.3, 71.7 (2 signals), 72.9, 73.4, 73.7, 75.7, 76.3, 77.3, 80.3 (C-2-C-6, C-2'-C-6', C-2''-C-6'', OCH_2 alkyl chain), 99.2, 101.8, 104.6 (C-1, C-1', C-1''), 172.6, 172.9 (C=O acetyl). HRMS: *m/z* calcd for (M-H)+ 811.4801; Found: 811.4782

Hexadecyl (3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-(1→4)-2,3,6-tri-*O*-benzoyl-D-galactopyranoside (36). Dimethyl(methylthio) sulfonium triflate (DMTST) (248 mg, 0.96 mmol) was added to a stirred mixture of **13** (204 mg, 0.240 mmol), cetyl alcohol (79 mg, 0.312 mmol) and powdered 4Å molecular

sieves in CH_2Cl_2 (8 mL). After 14 h at room temperature, triethylamine (1 mL) was added and the mixture was stirred for an additional 15 min before it was filtered through Celite and concentrated. Flash chromatography (toluene-EtOAc 6:1) yielded **36** (226 mg, 0.216 mmol, 90%), $[\alpha]_D$ +57.4°(*c* 1.0, $CHCl_3$). NMR data ($CDCl_3$): ^{13}C, δ 14.2 (CH_3 alkyl chain), 20.6, 20.7 (2 signals) (CH_3 acetyl), 22.7- 31.9 (alkyl chain C), 61.3 (C-6'), 62.2 (2 C's, C-6, C-2'), 68.1 (C-4'), 68.6 (C-5'), 69.6 (C-2), 70.3 (OCH_2 alkyl chain), 71.5 (C-3'), 72.3 (C-5), 73.5 (C-3), 76.3 (C-4), 99.1 (C-1', $J_{C-1, H-1}$ 169 Hz), 101.6 (C-1, $J_{C-1, H-1}$ 156 Hz), 128.3-133.7 (aromatic C), 165.2, 166.1 (2 C) (C=O benzoyl), 169.7, 169.9, 170.4 (C=O acetyl); ^1H, δ 0.88 (t, 3H, CH_3 alkyl chain), 1.0-1.53 (m, 28H, alkyl chain H), 1.95, 2.04, 2.08 (s, 9H, CH_3 acetyl), 3.55 (m, 1H, OCH_2 alkyl chain), 3.61-3.66 (m, 2H, H-2', H-6'), 3.93-4.04 (m, 2H, OCH_2 alkyl chain, H-6'), 4.12 (t, 1H, H-5), 4.38 (d, 1H, H-5'), 4.46 (d, 1H, H-4), 4.71-4.78 (m, 3H, H-1, H-6), 4.99-5.06 (m, 2H, H-1', H-4'), 5.35 (dd, 1H, H-3), 5.54 (t, 1H, H-3'), 5.67 (dd, 1H, H-2), 7.26-8.12 (m, 15H, aromatic H).

Anal. Calcd for $C_{55}H_{71}O_{16}N_3$: C, 64.13; H, 6.95; N, 4.08%. Found: C, 64.25; H, 7.01; N, 3.98%.

Hexadecyl (2-acetamido-2-deoxy-α-D-glucopyranosyl)-(1→4)-β-D-galactopyranoside (3). **36** (192 mg, 0.184 mmol) was dissolved in EtOAc:MeOH:HOAc 10:5:5 (5 mL) and Pd/C (10%, 25 mg) was added. The mixture was hydrogenated in a Parr apparatus (120 psi) for 24 h and then filtered through Celite and concentrated. The residue was dissolved in MeOH (8 mL) and treated with a catalytic amount of 1M NaOMe in MeOH solution After stirring at room temperature for 2 h the reaction was neutralised with Dowex 50 H^+, filtered and concentrated. After gel filtration on a Sephadex® LH-20-gel column eluted with MeOH compound **3** was obtained (51 mg, 0.085 mmol, 46%), $[\alpha]_D$ +68.6°(*c* 0.5, MeOH). NMR data (CD_3OD, 30 °C): ^{13}C, δ 14.4 (CH_3 alkyl chain), 22.6 (CH_3 acetyl), 23.7 (CH_2 alkyl chain), 27.0-33.0 (alkyl chain C), 55.5 (C-2'), 60.7, 62.3 (C-6, C-6'), 71.5, 72.0, 72.6, 72.7, 73.6, 74.5, 76.6, 77.6 (C-2-C-5, C-3'-C-5', OCH_2 alkyl chain), 100.2 (C-1'), 105.3 (C-1), 173.7 (C=O acetyl).

Anal. calcd. for $C_{30}H_{57}O_{11}N \cdot H_2O$: C, 57.58; H, 9.50; N, 2.24%. Found: C, 58.11; H, 9.20; N, 2.11%.

Hexadecyl (2-amino-2-deoxy-α-D-glucopyranosyl)-(1→4)-β-D-galactopyranoside (4). Compound **36** (327 mg, 0.313 mmol) was hydrogenated as described for **3**. The residue was then dissolved in 1M aq NaOH solution (9 mL) and refluxed for 15 h. The mixture was neutralised with 1M aq HCl, concentrated, and the residue was purified on a column of Sephadex® LH-20 gel (eluted with MeOH) to give **4** (72 mg, 0.128 mmol, 41 %), $[\alpha]_D$ +44.8°(*c* 1.0, MeOH). NMR data (CD_3OD, 30°C, pH 7): ^{13}C, δ 14.4 (CH_3 alkyl chain), 23.7-33.0 (alkyl chain C), 57.0 (C-2'), 60.8, 62.2 (C-6, C-6'), 71.3, 71.6, 72.6, 73.3, 74.2, 74.6, 75.8, 78.0 (C-2-C-5, C-3'-C-5', OCH_2

alkyl chain), 100.1 (C-1'), 105.2 (C-1). HRMS: *m/z* calcd for (M-H)+ 566.3904; Found: 566.3923

Pent-4-enyl (2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-3, 6-di-*O*-benzyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside (38). A mixture of 2,3,4,6-tetra-*O*-acetyl-α-D-galactosyl bromide **37** (96 mg, 233 mmol), pent-4-enyl 3,6-di-*O*-benzyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside **30**[30] (108 mg, 0.155 mmol), *sym*-collidine (18 μL, 0.139 mmol) and 4Å molecular sieves in CH_2Cl_2 (7 mL) was cooled to –35 °C. The mixture was stirred for 20 min and then AgOTf (119 mg, 0.465 mmol) was added. After 1 h triethylamine (1 mL) was added and the mixture was then allowed to attain room temperature before it was diluted CH_2Cl_2 (20 mL) and filtered through Celite. Flash chromatography of the residue (light petroleum-EtOAc 2:1) gave **38** (141 mg, 0.137 mmol, 88%) as a foam. $[\alpha]_D$ +26.4°(*c* 0.5, $CHCl_3$). NMR data ($CDCl_3$): ^{13}C, δ 20.6, 20.8, 21.0 (CH_3 acetyl), 28.5, 29.9 (CH_2 pentenyl) 56.4, 60.8, 67.0, 67.4, 68.7, 69.5, 70.6, 71.0, 73.7, 74.7, 75.2, 77.6, 78.3 (C-2-C-6, C-2'-C-6', OCH_2 pentenyl, CH_2 benzyl), 97.9 (C-1, $J_{C1,\ H\text{-}1}$ 163 Hz), 100.5 (C-1', $J_{C\text{-}1,\ H\text{-}1}$ 163 Hz), 114.8 (CH_2= pentenyl), 126.6-139.1 (aromatic C, CH= pentenyl), 162.4, 162.5 (C=O TCP), 169.2, 170.0, 170.2, 170.4 (C=O acetyl) ^1H δ 1.48-1.56 (m, 2H, pentenyl), 1.85-1.92 (m, 2H, pentenyl), 1.97, 2.01, 2.06 (s, 12H, CH_3 acetyl), 3.33 (m, 1H, OCH_2 pentenyl), 3.40-3.48 (m, 1H, H-5), 3.68-3.79 (m, 4H, OCH_2 pentenyl, H-6, H-5'), 3.96-4.18 (m, 5H, H-2, H-3, H-4, H-6'), 3.34, 4.50 (d, 2H, CH_2 benzyl), 4.55 (d, 1H, H-1' $J_{1,\ 2}$ 7.69 Hz) 4.75-4.87 (m, 5H, CH_2 benzyl 2H, pentenyl 2H, H-3') 5.05 (d, 1H, H-1 $J_{1,\ 2}$ 7.97 Hz), 5.14 (dd, 1H, H-2'), 5.29 (d, 1H, H-4'), 5.56-5.70 (m, 1H, pentenyl), 6.68-7.44 (m, 10H, aromatic H).

Anal. Calcd for $C_{47}H_{49}O_{16}NCl_4$: C, 55.04; H, 4.82; N, 1.36%. Found: C, 54.94; H, 4.80; N, 1.51%.

Hexadecyl (2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-tetrachlorophthalimido-β-D-glucopyranoside (39). Disaccharide **38** (540 mg, 0.526 mmol), cetyl alcohol (239 mg, 0.947 mmol), NIS (136 mg, 0.605 mmol) and TESOTf (131 μL, 0.579 mmol) were reacted and worked-up according to method a described for **35**. Flash chromatography (light petroleum-EtOAc 4:1) of the residue gave **39** (540 mg, 458 mmol, 87%), $[\alpha]_D$ +21.4°(*c* 0.5, $CHCl_3$). NMR data ($CDCl_3$): ^{13}C, δ 14.3 (CH_3 alkyl chain), 20.6 (2 signals), 20.7, 20.8, (CH_3 acetyl), 22.8-32.0 (alkyl chain C), 56.5 (C-2), 61.0, 67.1, 67.6, 69.6, 69.7, 70.6, 71.1, 73.8, 74.8, 75.2, 77.6, 78.4 (C-2-C-6, C-2'-C-6', OCH_2 alkyl chain, CH_2 benzyl), 98.0 (C-1, $J_{C\text{-}1,\ H\text{-}1}$ 168 Hz), 100.6 (C-1', $J_{C\text{-}1,\ H\text{-}1}$ 163 Hz), 126.7-139.6 (aromatic C), 162.3, 162.5 (C=O TCP), 169.3, 170.1, 170.2, 170.3 (C=O acetyl), ^1H, δ 0.88 (t, 3H, CH_3 alkyl chain), 0.99-1.39 (m, 28H, alkyl chain), 1.97, 2.01, 2.06 (s, 12H, CH_3 acetyl),

3.30-3.38 (m, 2H, CH_2 alkyl chain), 3.44-3.49 (m, 1H, H-5), 3.69-3.76 (m, 4H, OCH_2 alkyl chain, H-6, H-5') 3.97-4.16 (m, 5H, H-2, H-3, H-4, H-6'), 4.34 (d, 1H, CH_2 benzyl), 4.50 (d, 1H, CH_2 benzyl), 4.55 (d, 1H, H-1' $J_{1,2}$ 7.97 Hz), 4.74 (d, 1H, CH_2 benzyl), 4.81 (d, 1H, CH_2 benzyl), 4.85 (dd, 1H, H-3'), 5.03 (d, 1H, H-1 $J_{1,2}$ 7.97 Hz) 5.13 (dd, 1H, H-2'), 5.29 (d, 1H, H-4'), 6.68-7.42 (m, 10H, aromatic H).

Anal. Calcd for $C_{58}H_{73}O_{16}NCl_4$: C, 58.94; H, 6.23; N, 1.18%. Found: C, 58.71; H, 6.13; N, 1.31%.

Hexadecyl (2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside (40). A solution of **39** (410 mg, 0.347 mmol) and ethylenediamine (463 μL, 6.94 mmol) in CH_3CN-EtOH-THF 2:1:1 (10 mL) was stirred for 22 h at 60 °C. The mixture was then concentrated and co-concentrated twice with toluene. Purification by flash chromatography ($CHCl_3$-MeOH 15:1+1% triethylamine) gave material (188 mg, 0.253 mmol, 73 %) having NMR data ($CDCl_3$): ^{13}C, δ 14.2 (CH_3 alkyl chain), 22.8-32.0 (alkyl chain C), 56.6, 62.3, 68.5, 69.2, 70.1, 72.0, 73.5, 73.8, 74.4, 74.8, 75.2, 76.9, 83.3 (C-2-C-6, C-2'-C-6', OCH_2 alkyl chain, CH_2 benzyl), 102.9, 103.5 (C-1, C-1'), 127.8-138.6 (aromatic C). The compound was dissolved in EtOAc-MeOH 1:2 (8 mL) and acetic acid (0.5 mL) and Pd/C (10%, 30 mg) were added. The mixture was hydrogenated (120 psi) for 48 h and then neutralised with triethylamine, filtered through Celite and concentrated. The residue was dissolved in pyridine (3 mL) and treated with Ac_2O (2 mL). After stirring at room temperature for 12 h the reaction mixture was concentrated and the residue purified (Flash chromatography $CHCl_3$-MeOH 10:1) which yielded **40** (85 mg, 0.099 mmol, 29%), $[\alpha]_D$ –8.5°(*c* 1.0, $CHCl_3$). NMR data ($CDCl_3$): ^{13}C, δ 14.1 (CH_3 alkyl chain), 20.5-21.4 (6 signals, CH_3 acetyl), 22.7 (CH_3 *N*-acetyl), 23.3-32.0 (alkyl chain C), 53.2, 60.8, 62.5, 66.7, 69.1, 69.8, 70.8, 70.9, 72.3, 72.6, 75.7 (C-2-C-6, C-2'-C-6', OCH_2 alkyl chain), 100.9, 101.0 (C-1, C-1'), 169.5-171.0 (C=O acetyl), ^1H, δ 0.88 (t, 3H, CH_3 alkyl chain), 0.99-1.39 (m, 28H, alkyl chain), 1.97 (2 signals), 2.08 (2 signals), 2.00, 2.06, 2.12 (s, 21H, CH_3 acetyl), 3.26-3.34 (m, 1H, OCH_2 alkyl chain), 3.51-3.55 (m, 1H, H-5), 3.64-3.79 (m, 3H, OCH_2 alkyl chain, H-4, H-5'), 3.90-4.12 (m, 4H, H-2, H-6, H-6'), 4.31-4.41 (m, 3H, H-1 $J_{1,2}$ 7.14 Hz, H-1' $J_{1,2}$ 7.97 Hz, H-6'), 4.86 (dd, 1H, H-3'), 4.94-5.04 (m, 2H, H-3', H-2), 5.24 (d, 1H, H-4'), 5.45 (d, 1H, HNAc). HRMS: *m/z* calcd for (M-H)+, 860.4644; Found: 860.4660

Octyl (2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-tetrachlorophtalimido-β-D-glucopyranoside (41). Disaccharide **38** (710 mg, 0.692 mmol), *n*-octanol (328 μL, 2.08 mmol), NIS (179 mg, 0.796 mmol) and TESOTf (172 μL, 0.761 mmol) were reacted and worked-up according to method a described for **35**. Flash chromatography (light petroleum-EtOAc 4:1-2:1) of

the residue yielded **41** (660 mg, 0.609 mmol, 88%), $[\alpha]_D$ +33.0°(*c* 0.2, $CHCl_3$). NMR data ($CDCl_3$): ^{13}C, δ 14.2 (CH_3 alkyl chain), 20.6 (2 signals), 20.7, 20.8 (CH_3 acetyl), 22.7-31.8 alkyl chain C), 56.4, 60.9, 67.0, 67.5, 69.5, 69.6, 70.6, 71.0, 73.7, 74.8, 75.2, 77.6, 78.4 (C-2-C-6, C-2'-C-6', OCH_2 alkyl chain, CH_2 benzyl), 98.0 (C-1, $J_{C\text{-}1,\ H\text{-}1}$ 164 Hz), 100.6 (C-1', $J_{C\text{-}1,\ H\text{-}1}$ 161 Hz), 126.6-129.6 (aromatic C), 162.3, 162.5 (C=O TCP), 169.1, 170.0, 170.2, 170.4 (C=O acetyl), ^1H, δ 0.80 (t, 3H, CH_3 alkyl chain), 0.83-1.40 (m, 12H, alkyl chain), 1.99, 2.02, 2.06, 2.07 (s, 12H, CH_3 acetyl), 3.32-3.40 (m, 1H, CH_2 alkyl chain), 3.46-3.49 (m, 1H, H-5), 3.68-3.77 (m, 4H, CH_2 alkyl chain, H-5', H-6), 3.99-4.19 (m, 5H, H-2, H-3, H-4, H-6''), 4.35 (d, 1H, CH_2 benzyl), 4.50 (d, 1H, CH_2 benzyl), 4.56 (d, 1H, H-1' $J_{1,\ 2}$ 7.97 Hz), 4.76 (d, 1H, CH_2 benzyl), 4.82 (d, 1H, CH_2 benzyl), 4.88 (dd, 1H, H-3'), 5.05 (d, 1H, H-1' $J_{1,\ 2}$ 7.97Hz), 5.15 (dd, 1H, H-2') 5.30 (d, 1H, H-4'), 6.68-7.41 (m, 10H, aromatic H).

Anal. Calcd for $C_{50}H_{57}O_{16}NCl_4$: C, 56.14; H, 5.37; N, 1.31. Found: C, 55.75; H, 5.26; N, 1.49%.

Octyl (β-D-galactopyranosyl)-(1→4)-2-amino-2-deoxy-β-D-glucopyranoside (6). A solution of **41** (149 mg, 0.136 mmol) and ethylenediamine (272 μL, 4.08 mmol) in CH_3CN-EtOH-THF 2:1:1 (7 mL) was stirred for 24 h at 60 °C. The mixture was then concentrated and co-concentrated twice with toluene. The residue was purified using a short silica gel column ($CHCl_3$-MeOH 10:1). The obtained compound was dissolved in EtOAc-MeOH 1:1 (4 mL) and 0.5 mL H_2O and Pd/C (10%, 20 mg) was added. The mixture was hydrogenated (120 psi) for 48 h, filtered through Celite and concentrated. The residue was purified by a Sephadex® LH-20 column with MeOH as eluent to give **6** (49 mg, 0.104 mmol, 76%) as a glassy solid, $[\alpha]_D$ -1.4°(*c* 1.0, MeOH). NMR data (CD_3OD, 35°C, pH 7): ^{13}C, δ 14.4 (CH_3 alkyl chain), 23.7-33.0 (alkyl chain C), 57.5, 61.7, 62.5, 70.2, 71.0, 72.5, 73.6, 74.8, 76.7, 77.0, 81.0 (C-2-C-6, C-2'-C-6', OCH_2 alkyl chain), 101.5 (C-1), 105.2 (C-1'). HRMS: *m/z* calcd for (M-H)+ 454.2652; Found: 454.2674.

Octyl (β-D-galactopyranosyl)-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranoside (5). Compound **41** (182 mg, 0.169 mmol) and ethylenediamine (338 μL, 5.07 mmol) in CH_3CN-EtOH-THF 2:1:1 (7 mL) was reacted and worked-up as described for **6**. The compound, obtained after flash chromatography ($CHCl_3$-MeOH 10:1), was dissolved in MeOH (5 mL) and Ac_2O (52 μL, 0.554 mmol) was added. After stirring at room temperature for 3 h the mixture was concentrated. The remaining residue was dissolved in EtOAc-MeOH 1:1 (4 mL) and 0.5 mL H_2O and Pd/C (10%, 15 mg) was added. The mixture was hydrogenolysed (120 psi) for 48 h, filtered through Celite and concentrated. Purification using a Sephadex® LH-20 column (MeOH) gave **5** (60 mg, 0.117 mmol, 69%), $[\alpha]_D$ –1.4°(*c* 1.0, MeOH). NMR data (CD_3OD, 35°C): ^{13}C, δ 14.4

(CH_3 alkyl chain), 23.7-33.0 (alkyl chain C), 56.8, 62.1, 62.6, 70.4, 70.8, 72.7, 74.3, 74.9, 76.6, 77.1, 81.2 (C-2-C-6, C-2'-C-6', OCH_2 alkyl chain), 102.8 (C-1,), 105.1 (C-1'), 173.5 (C=O acetyl). HRMS: *m/z* calcd for (M-H)+ 496.2758; Found: 496.2781

ACKNOWLEDGMENT

This work was supported by the Swedish Natural Science Research Council.

REFERENCES

1. F. Maisonrouge-McAuliffe and E. A. Kabat, *Arch. Biochem. Biophys.*, **175**, 71 (1976).
2. F. Maisonrouge-McAuliffe and E. A. Kabat, *Arch. Biochem. Biophys.*, **175**, 81 (1976).
3. F. Maisonrouge-McAuliffe and E. A. Kabat, *Arch. Biochem. Biophys.*, **175**, 90 (1976).
4. E. F. Hounsell, A. M. Lawson, M.S. Stoll, D. P. Kane, G. C. Cashmore, R. A. Carruthers, J. Feeny and T. Feizi, *Eur. J. Biochem.*, **186**, 597 (1989).
5. H. Paulsen and D. Scnell, *Chem. Ber.*, **114**, 333 (1982).
6. C. Tanford, *The Hydrophobic Effect: Formation of Micelles and Biological Membranes*; John Wiley & Sons, Inc 1973.
7. J-H, Fuhrhop and B. Rosengarten, *Synlett*, 1015 (1997).
8. P. J. Garegg and S. Oscarson, *Carbohydr. Res.*, **136**, 207 (1985).
9. J. Fried and D. E. Walz, *J. Am. Chem. Soc.*, **71**, 140 (1949).
10. R. U. Lemieux and *Can. J. Chem.*, **29**, 1079 (1951).
11. D. Wagner and J. P. H. Verheyden, J. G. Moffatt, *J. Org. Chem.*, **39**, 24 (1974).
12. M. A. Nashed and L. Anderson, *Tetrahedron Lett.*, 3503 (1976).
13. R. F. Helm and J. Ralph, *J. Org. Chem.*, **56**, 7015 (1991).
14. C. J. Cavender and V. J. Jr. Shiner, *J. Org. Chem.*, **37**, 3567 (1972).
15. J. Zaloom and D. C. Roberts, *J. Org. Chem.*, **46**, 5173 (1981).
16. A. Vasella, C. Witzig, J-L. Chiara and M. Martin-Lomas, *Helv. Chim. Acta*, **74**, 2073 (1991).
17. T. Buskas, P, J. Garegg, P. Konradsson and J-L. Maloisel , *Tetrahedron: Asymmetry*, **5**, 2187 (1994).
18. K. Ekelöf and S. Oscarson, *J. Org. Chem.*, **61**, 7711 (1996).
19. S. Hanessian and J. Banoub, *Carbohydr. Res.*, **53**, C13 (1977).
20. D. Horton, *Methods Carbohydr. Chem.* VI, 282 (1972).
21. B. Helferich and J. Zirner, *Chem. Ber.*, **95**, 2604 (1962).
22. P. J. Garegg, H. Hultberg and S. Wallin, *Carbohydr., Res.* **108**, 97 (1982).
23. P. Fügedi, P. J. Garegg,H. Lönn and T. Norberg, *Glycoconjugate J.*, **4**, 97 (1987).
24. J. O. Kihlberg, D. A. Leigh and D. R. Bundle, *J. Org. Chem.*, **55**, 2860 (1990).
25. L. Blomberg and T. Norberg, *J. Carbohydr. Chem.*, **11**, 751 (1992).
26. R. R. Schmidt and J. Michel, *Angew. Chem. Int. Ed. Eng.*, **19**, 731 (1980).
27. R. R. Schmidt and W. Kinzy, *Adv. Carbohydr. Chem. Biochem.*, **50**, 21 (1994).
28. P. Fügedi and P. J. Garegg, *Carbohydr. Res.*, **149**, C9 (1986).
29. J. Kerékgyártó, G. M. van der Ven, J. P. Kamerling, A. Lipták and J. F. G. Vliegenthart, *Carbohydr. Res.*, **238**, 135 (1993).

30. J. S. Debenham, S. D. Debenham and B. Fraser-Reid, *Bioorg. Med. Chem.*, **4**, 1909 (1996).
31. B. Fraser-Reid, U. E. Udodong, Z. Wu, H. Ottoson, J. R. Merrit, C. S: Rao, C. Roberts and R. Madsen, *Synlett*, 927 (1992).
32. R. Madsen and B. Fraser-Reid, *Modern Methods in Carbohydrate Chemistry*; Harwood Academic Publishers: Switzerland 1995.
33. J. S. Debenham, R. Rodebaugh and B. Fraser-Reid, *J. Org. Chem.*, **62**, 4591 (1997).
34. Y-M. Zhang, A. Brodzky, P. Sinaÿ, G. Saint-Marcoux and B. Perly, *Tetrahedron: Asymmetry*, **6**, 1195 (1995).
35. R. K. Jain and K. L. Matta, *Carbohydr. Res.*, **226**, 91 (1992).
36. A. Toepher and R. R. Schmidt, *J. Carbohydr. Chem.*, **12**, 809 (1993).
37. S. Numomura, M. Iila, M. Numata, M. Sugimoto and T. Ogawa, *Carbohydr. Res.*, **263**, C1 (1994).
38. P. V. Nikrad, M. A. Kashem, K. B. Wlasichuk, G. Alton and A. P. Venot, *Carbohydr. Res.*, **250**, 145 (1993).
39. A. Kameyama, H. Ishida, M. Kiso and A. Hasegawa, *J. Carbohydr. Chem.*, **13**, 641 (1994).
40. R. K. Jain, R. D. Locke, A. Mohammad and K. L. Matta, *J. Chem. Soc., Chem. Commun.*, 65 (1996).
41. G. V. Reddy, R. K. Jain, R. D. Locke and K. L. Matta, *Carbohydr. Res.*, **280**, 261 (1996).
42. T. Ehara, A. Kameyama, Y. Yamada, H. Ishida, M. Kiso and A. Hasegawa, *Carbohydr. Res.*, **281**, 237 (1996).
43. U. Ellervik and G. Magnusson, *J. Org. Chem.*, **63**, 9314 (1998).
44. T. Buskas, B. Fraser-Reid, P. Konradsson and E. Söderberg, BP275, *XIX International Carbohydrate Symposium*, San Diego, 1998.
45. G. Zemplén, *Chem. Ber.*, **55**, 2860 (1926).
46. L. Öhberg, Doctoral Thesis, Stockholm University: Stockholm, 1998.
47. C. Pale-Grosdemange, E. S. Simon, K. L. Prime and G. M. Whitesides, *J. Am. Chem. Soc.*, **113**, 12 (1991).
48. D. Boumrah, M. M. Campbell, S. Fenner and R. G. Kinsman, *Tetrahedron Lett.*, **32**, 7735 (1991).