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SYNTHESIS OF A PENTASACCHARIDE AND A HEPTASACCHARIDE CORRESPONDING TO AN OVARIAN GLYCOPROTEIN; STUDIES TOWARDS GLYCOSYLATIONS

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Abstract. The syntheses of pentasaccharide **I** and heptasaccharide **II**, which correspond to an ovarian O-glycoprotein, are presented. The protected pentasaccharide **1** was prepared by condensing a trisaccharide donor (**18c**) with a disaccharide acceptor (**8b**), while condensation of the same trisaccharide donor (**18c**) with a tetrasaccharide acceptor (**25b**) provided the protected heptasaccharide **2**. Special attention was paid to the deblocking of the protected derivatives **1** and **2** to give **I** and **II**, respectively. The β-bonds in **8b** and **25b** were prepared by using glycosyl donors with *non*-participating groups at C-2, which were earlier applied for the synthesis of α-glycosides. For the synthesis of the trisaccharide donor (**18c**), condensations of several activated Galα(1->3)Gal disaccharides with protected GlcNAc residues were compared. It was found that the α/β ratio and the yield of this glycosylation are influenced by the leaving group at the anomeric centre, the character of the participating acyl group and, in particular, by the unfavourable steric interaction between donor and acceptor. In order to reduce this steric interaction between donor and acceptor, the conformation of the GlcNAc acceptor was changed to the 1,6-anhydro derivative **16**, which afforded in the glycosylation with glycosyl bromide **13c** a high yield of the desired trisaccharide **17**.

Introduction

Until some decades ago, the biological role of the carbohydrate content of glycoconjugates remained elusive. Recent findings in cell biology indicated a crucial role for carbohydrates in the regulation of biological processes such as intercellular recognition and adhesion[1], anti-blood coagulation[2] and cellular differentiation[3]. In many instances, the carbohydrate part of glycoconjugates may function as an antigenic determinant, as is the case for blood-group determinants[4]. The chemical structures corresponding to the human A, B, H(O), Le^a, Le^b, I and i blood-group determinants, which, for example, can be isolated from human ovarian cyst fluid, are now well established[5].

The functional relevance of glycoconjugates is not only reflected in numerous biological studies but also in the huge research effort directed towards the chemical synthesis of these complex carbohydrates. Advanced glycosylation procedures and protective group strategies in particular have proved to be excellent tools for successful synthesis of oligosaccharides. The synthesis of each distinct oligosaccharide derivative, however, requires the preparation of a new set of suitably protected building blocks, since structural variation among oligosaccharides is enormous. In order to reduce the number of different building blocks in oligosaccharide synthesis, we started to study the use of 'universal building blocks'

(*vide infra*).

Despite the fact that much attention has been paid to the development of new methods for the introduction of glycosidic bonds, in many instances glycosylations proceed unsatisfactory. In this respect it should be stressed that it is difficult to predict the yield and stereochemical outcome of any particular glycosylation because a large number of factors can play a role. For example it is known that the characteristics of the protective groups on the glycosyl donor and acceptor can exert an enormous effect on the glycosylation[6-9]. Furthermore it was shown that the solvent can exert a decisive influence on the α/β ratio and the yield of a glycosylation[10-12]. Recently, we revealed that in some cases the glycosylation is governed by the steric interaction of donor and acceptor in the transition state leading to either the α- or β-glycosidic bond[13]. Other factors that have clearly shown to act on glycosylations are the type of the leaving group at the anomeric centre, the group at C-2 of the glycosyl donor, the promoter and the temperature.

This paper is concerned with the chemical synthesis of a pentasaccharide and heptasaccharide fragment corresponding to an ovarian O-glycoprotein fragment (Fig.1), displaying structural elements of the human ABO blood-group determinants. Similar structural features are present in tumour-associated antigens[14] and in the carbohydrate component of the murine and porcine Zonae Pellucidae[15]. The target oligosaccharides contain the core structure fragment of human ovarian blood-group substances, β-D-Gal(1-3)-β-D-GlcNAc-β-(1-3)[β-D-Gal(1-4)-β-D-GlcNAc-β-(1-6)]-D-Gal[14]. The type I chain, β-D-Gal(1-3)-β-D-GlcNAc, is extended at the non-reducing end with an α-D-Gal(1-3) residue giving a B-determinant, whereas for the heptasaccharide the β-D-Gal(1-4)-β-D-GlcNAc is provided with a terminal β-D-GlcNAc(1-3) linkage giving an elongated type II chain as described by Dua et al[16]. The pentasaccharide and the heptasaccharide are both provided with an amine-containing linker in order to facilitate the formation of a neo-glycoprotein or a neo-glycolipid.

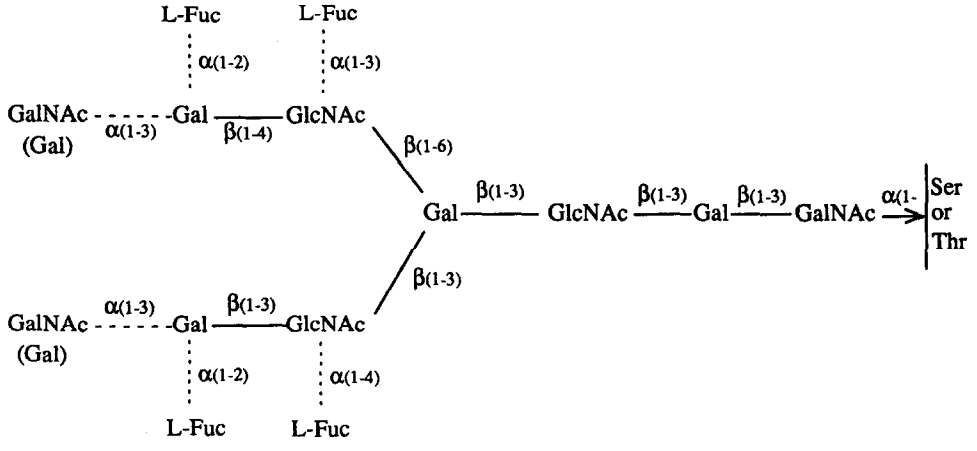
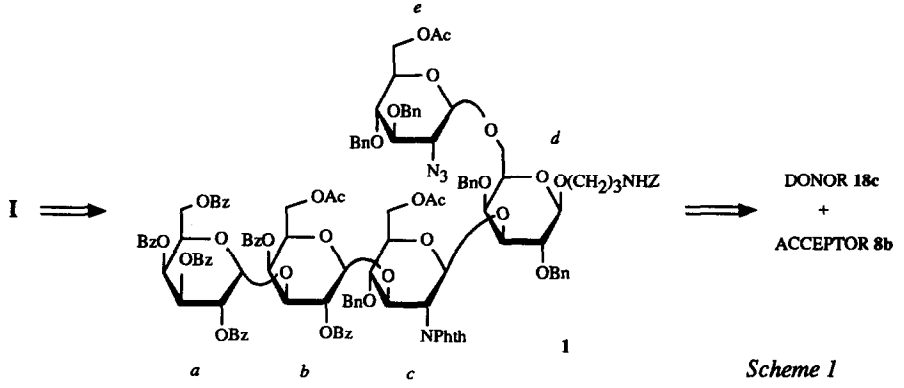


Fig.1 Ovarian O-Glycoprotein fragments

Results and discussion

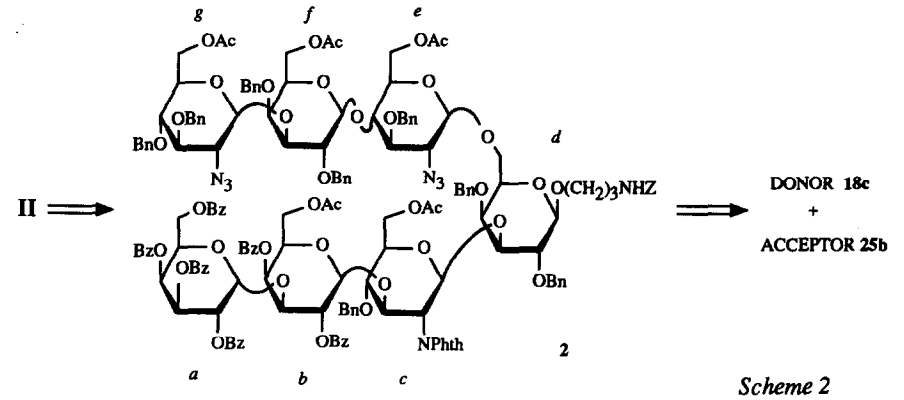
General Strategy

Here we report the synthesis of pentasaccharide **I** (Scheme 6) and heptasaccharide **II** (Scheme 8). For the synthesis of the oligosaccharides we devised a strategy in which one common trisaccharide donor (**18c**) was used for the preparation of both compounds. For the synthesis of the pentasaccharide we prepared a disaccharide acceptor (**8b**) which could be condensed with the trisaccharide donor (**18c**) to give the protected pentasaccharide (Scheme 1).



Scheme 1

In order to obtain the protected heptasaccharide, the same trisaccharide donor (**18c**) was coupled with a tetrasaccharide acceptor (**25b**) (Scheme 2).



Scheme 2

The amino group of the spacer moiety is protected with a benzyloxycarbonyl group, which can be removed in the last step by hydrogenolysis. The acetylamino group of the trisaccharide donor (**18c**) was masked by a participating phthalimido group. This group was chosen because we anticipated that a participating group was necessary for a successful β-coupling between the relatively large (and therefore less reactive)

trisaccharide donor and di- or tetrasaccharide acceptor. The acetylamino groups of the di- and tetrasaccharide acceptors were masked by (non-participating) azido groups. The azido group is stable under a great number of conditions and the deblocking of this group generally proceeds smoothly. The two β-glucosamine linkages of the tetrasaccharide acceptor and the β-glucosamine linkages of the disaccharide acceptor were introduced by using insoluble silver salt promoters. The azido containing building blocks here used for β-glycosylation, have been used previously for α-glycosylation; we call this strategy the 'universal building block' approach[17].

The most established method for the introduction of β-linkages in the glucosamine- and galacto-series takes advantage of a participating group at C-2 of the glycosyl donor. On the other hand, for the synthesis of an α-glycosidic bond in the same series a non-participating group at C-2 is required. Consequently, a typical β-glycosyl donor, containing a participating group at C-2, cannot be used for the introduction of an α-linkage. Nevertheless as various glycoconjugates contain gluco- and galactopyranoses in either α or β configuration, it would be of particular advantage to have only one type of glycosyl donor that may be coupled either α or β, by adjusting only the glycosylation conditions (Fig.2).

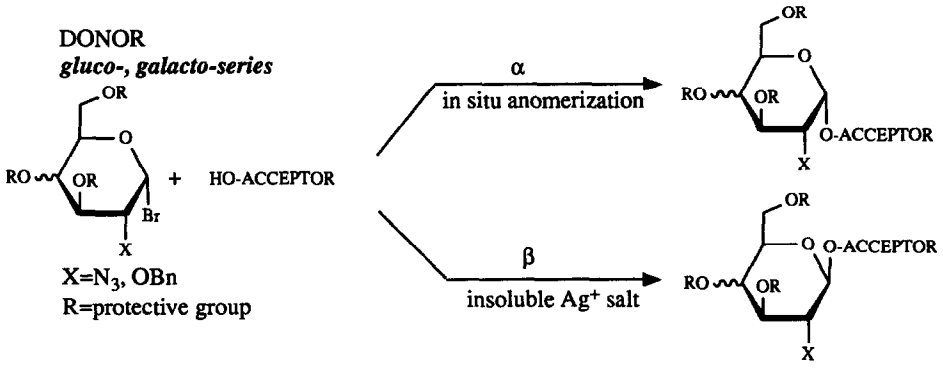


Fig. 2 'Universal building block' approach.

In principle such a universal approach is possible when using glycosyl bromides containing non-participating groups at C-2. Thus, glycosylations with glycopyranosyl bromides under 'in situ anomerization' conditions provide the α-gluco- or α-galactopyranosides, whereas an insoluble silver salt promotes (despite the presence of a non-participating group at C-2) the formation of the corresponding β-coupled glycosides.

The formation of α-glycosides via the 'in situ anomerization' procedure is generally applied, whereas the application of insoluble silver salts for the formation of β-linkages is less common and more delicate. In our group the use of insoluble silver salt promoters has been studied in much detail[7-9,17].

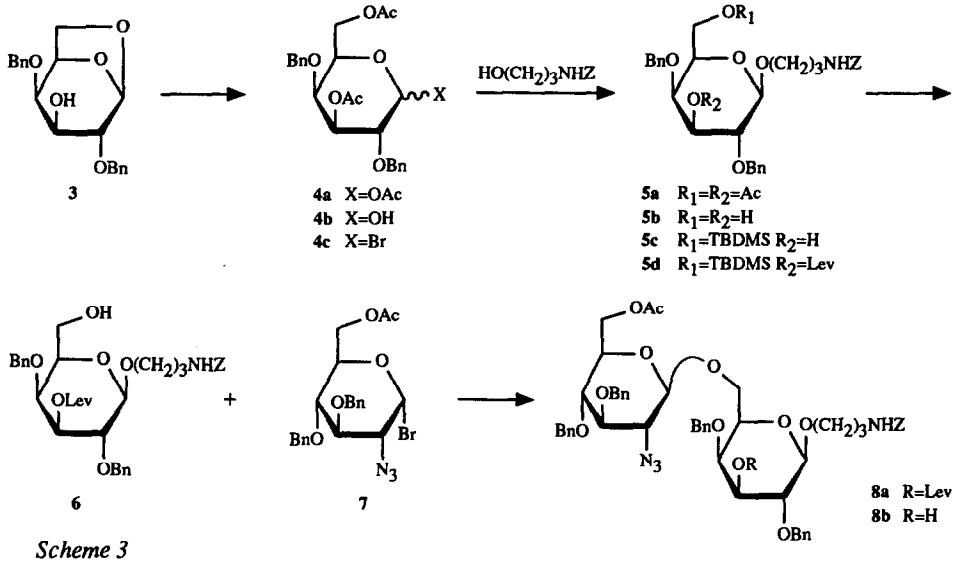
Recently, alternative methods for β-glycosylations which allow a similar universal building block strategy have been described. For example, Schmidt[18] reported the direct inversion of α-imidates in the presence of boron trifluoride etherate to give the corresponding β-glycosides. Furthermore it was reported that glycosyl donors containing an *n*-pentenyloxy[10], a thioalkyl[11] or a trichloracetimidate[12] group at the anomeric centre (in combination with a non-participating group at C-2) could be coupled either α or β depending on the solvent in which the reaction was conducted.

SYNTHESIS OF PENTASACCHARIDE I

Synthesis of glycosyl acceptor 8b

The synthetic route to the glycosyl acceptor **8b** is illustrated in Scheme 3. Thus, treatment of the known 2,4-di-O-benzyl-1,6-anhydro-β-D-galactopyranose[19] (**3**) with a mixture of trifluoroacetic acid and acetic anhydride and subsequent anomeric saponification with hydrazine acetate in N,N-dimethylformamide[20] gave **4b** (yield 97%), which was converted into the α-bromide **4c**[19] by the action of the Vilsmeier reagent (N,N-dimethylbromoforminium bromide)[21].

Condensation of the galactosyl bromide **4c** with 3-N-(benzyloxycarbonylamino)-1-propanol[22] in the presence of silver silicate-aluminate[23] afforded the β-coupled compound **5a** in 82% yield. Saponification of **5a** with potassium carbonate in dioxane/methanol gave the diol **5b** in quantitative yield.



Scheme 3

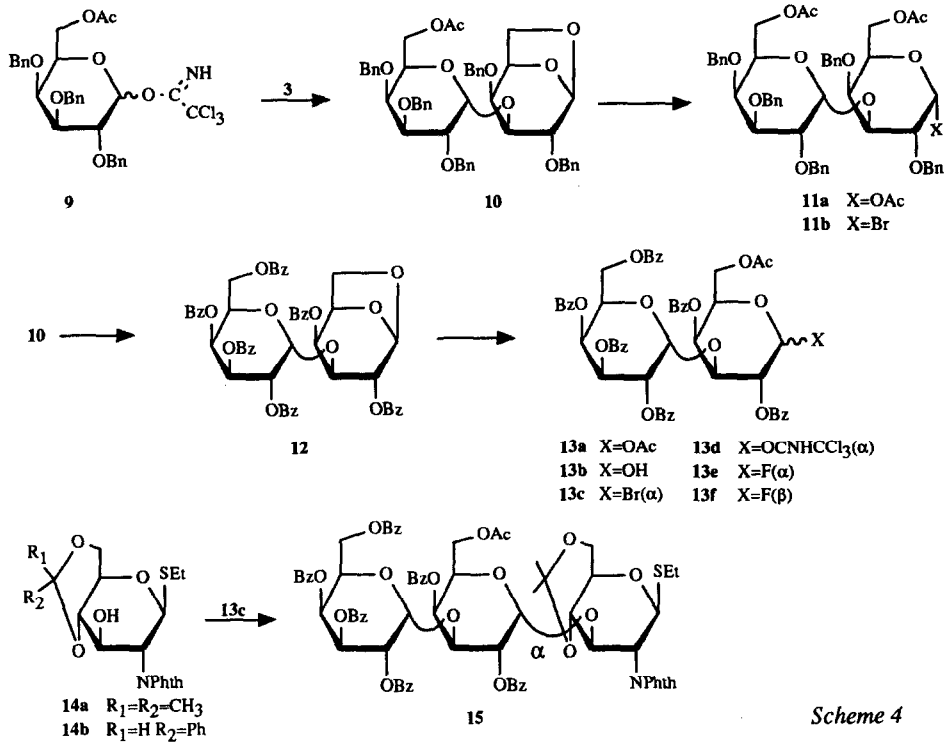
In the first approach to the synthesis of disaccharide **8b**, compound **5b** was coupled with glycosyl bromide **7**[24] in the presence of an insoluble silver salt. Quite unexpectedly this glycosylation afforded a complex mixture of isomers. Besides the formation of the desired β(1-6) coupled dimer (**8b**), α(1-6), β(1-3) and α(1-3) linked dimers were isolated. In order to improve the yield of the desired product, we decided to prepare glycosyl acceptor **6**, having a temporary protective group at C-3. To this end, the primary hydroxyl group of **5b** was selectively protected with a *tert*-butyldimethylsilyl (TBDMS) group to give **5c**. Next the free hydroxyl group was protected with a levulinoyl ester (**5d**) after which the TBDMS group was removed by acid treatment to give **6** in an overall yield of 88%.

Glycosylation of **6** with glycosyl donor **7** in the presence of silver silicate-aluminate gave **8a** in a β/α ratio of 4/1 (yield 43%). Cleavage of the levulinoyl group of compound **8a** with hydrazine acetate in pyridine afforded the glycosyl acceptor **8b**.

Synthesis of glycosyl donor **18c**, *studies towards the* β*-glycoside formation*

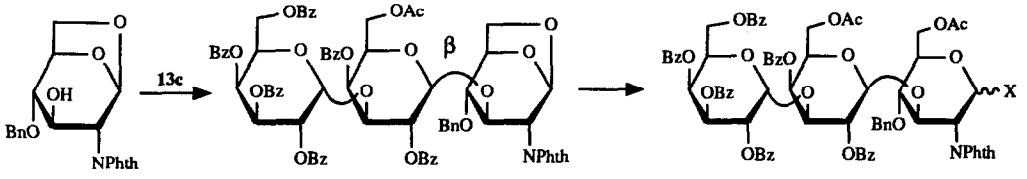
In order to prepare the glycosyl donor **18c**, glycosyl trichloroacetimidate **9** was coupled with the earlier used glycosyl acceptor **3** in the presence of trimethylsilyl trifluoromethanesulfonate (TMSOTf) to afford compound **10** in 70% yield (α/β ratio 7/1)(Scheme 4). Acetolysis of **10** and subsequent treatment with titanium tetrabromide[25] furnished compound **11b**. However, condensation of compound **11b** with acceptor **14a** in the presence of silver silicate-aluminate did not afford any coupled product. We assumed that the hydroxyl group of **14a** was not sufficiently reactive for this particular silver silicate-aluminate promoted coupling reaction. Therefore we decided to prepare a glycosyl donor containing a participating ester group at C-2 and to use a reactive glycosylation method. For this purpose the benzylated disaccharide **10** was converted into the benzoylated derivative **12**, by successive saponification of the 6'-O-acetyl group, hydrogenolysis and benzoylation of the hydroxyl groups with benzoyl chloride in pyridine. Acetolysis of **12** afforded compound **13a** which was then converted into various glycosyl donors (**13c-13f**).

In the next attempt to synthesize the desired trisaccharide, the benzoylated α-bromide (**13c**) was condensed with acceptor **14a** in the presence of silver trifluoromethanesulfonate (AgOTf) and 2,6-di-*tert*-butylpyridine at -50 °C in dichloromethane. Unexpectedly, this coupling reaction gave *exclusively the* α*-coupled* product (**15**) in 23% yield. Thus, despite the fact that a participating group is present at C-2 of the donor to direct the β-glycoside formation, only the α-interglycosidic bond was formed.



Scheme 4

We reasoned that the unexpected formation of this α-linkage was due to an unfavourable steric interaction between the glycosyl donor and glycosyl acceptor in the transition state leading to the β-interglycosidic bond. This assumption was confirmed by studying double stereodifferentiation in related carbohydrate coupling reactions[13]. In order to synthesize the required interglycosidic β-bond, we reasoned that we had to diminish the unfavourable steric interaction between the donor and acceptor in the β-transition state. With this in mind, 1,6-anhydro-4-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**16**) was chosen as glycosyl acceptor, because its 3-hydroxyl group has a different spatial orientation towards the bulky protective groups than the hydroxyl group of **14a**. Indeed, when **13c** was coupled with **16** in the presence of AgOTf only β-coupled trisaccharide (**17**) was formed in 75% yield (Scheme 5).



16 **17** **18a** X=OAc **18c** X=$OCNHCCl_3$ **18b** X=OH **18d** X=Cl

Scheme 5

The trisaccharide **17** was now smoothly converted to the glycosyl donor **18c** by acetolysis, anomeric saponification with hydrazine acetate and subsequent treatment with trichloroacetonitrile and potassium carbonate.

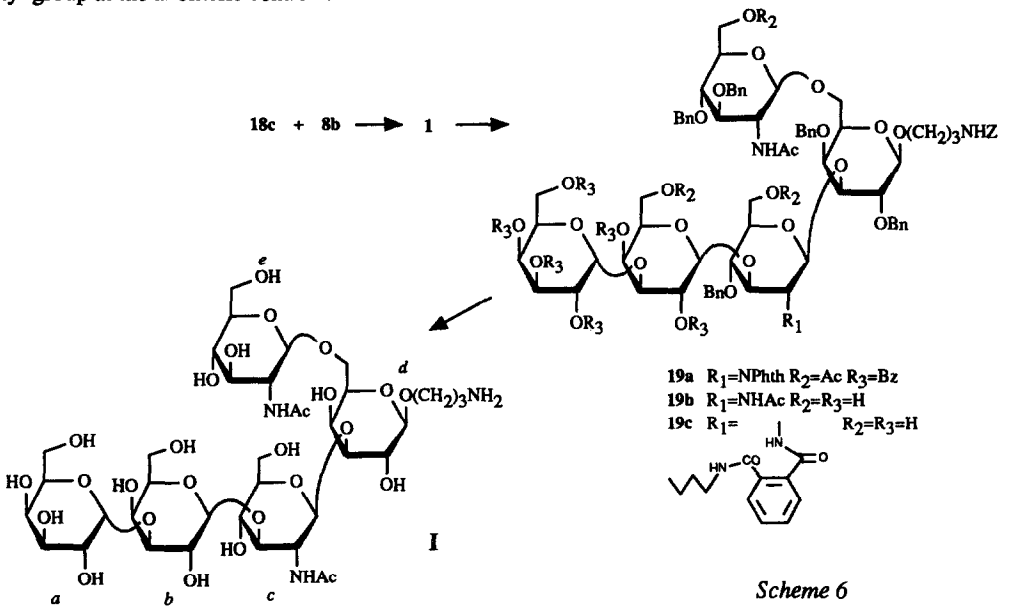
We then turned our attention again to the notorious β-coupling between a D-galactosyl donor, containing a participating ester group at C-2, and the 3-hydroxyl function of a 2-deoxy-2-phthalimido-D-glucosyl acceptor in the $^4C_1$ conformation. It was already reported by others that this particular coupling reaction is difficult to achieve. For instance, Ogawa et al.[26] reported a coupling reaction between 2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl trichloroacetimidate and allyl 6-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside catalysed by boron trifluoride etherate ($BF_3.Et_2O$), leading to β(1->4), β(1->3) and α(1->3) coupled disaccharides. The desired β(1->3) coupled product was isolated in only 2% yield, but surprisingly, the α(1->3) coupled disaccharide was formed in 29% yield.

On the other hand, it was reported by Wong et al.[27] that coupling reaction of the same galactopyranosyl imidate with allyl 4,6-O-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranoside, catalysed by TMSOTf, furnished 70% of the desired β(1->3) coupled product. This result prompted us to perform glycosylations with the benzoylated α-imidate **13d** and the corresponding peracetylated α-imidate. Coupling reactions of these glycosyl donors with acceptor **14b**[28] in the presence of TMSOTf furnished indeed β-coupled trisaccharide in 10% and 31% yield, respectively. As coupling reactions of glycosyl donors with a participating benzoyl group instead of an acetyl group give, in general, higher yields of 1,2-trans glycosides[29], it is remarkable that the coupling of the acetylated imidate is the most successful one.

Finally, we tried to condense the α- and β-fluorides **13e** and **13f** with acceptors **14a** and **14b**, respectively, in the presence of excess $BF_3.Et_2O$. However, no glycosylation products were detected. It should be concluded that for this particular coupling reaction the fluoride is not reactive enough.

Synthesis of the fully protected pentasaccharide 1 and its deprotection to give I (Scheme 6)

The fully protected pentasaccharide **1** (Scheme 1) was obtained in 44% yield by condensation of glycosyl donor **18c** with glycosyl acceptor **8b** in the presence of a catalytic amount of TMSOTf at 0 °C in dichloromethane. An important side-product of this reaction was a compound having a slightly higher R_f-value than the starting glycosyl imidate. Probably this compound arises from reaction of the anomeric centre of the activated donor with a trichloroacetimidate group to give a product containing an N-trichloroacetyl group at the anomeric centre[30].



Scheme 6

Having the fully protected pentasaccharide at our disposal, it had to be converted to the desired deprotected derivative. The first deprotection step was the reduction of the azido group with hydrogen sulphide in a mixture of pyridine and water[32]. Subsequent acetylation in a mixture of pyridine and acetic anhydride furnished crude **19a**. This compound was eluted from a sephadex LH 20 column to remove some impurities having a low molecular weight and which were formed during the reduction of the azido group.

In order to cleave the phthalimido group and to saponify the ester groups simultaneously, crude **19a** was treated with *n*-butylamine in methanol at reflux temperature for 96 hours[33]. In this respect it should be mentioned that treatment of a model compound, containing an N-benzyloxycarbonyl group, with hydrazine in methanol at 65 °C gives rise to some cleavage of the benzyloxycarbonyl group. Since the previous conditions are milder, cleavage of the phthalimido group with *n*-butylamine requires a prolonged reaction time and even after 96 hours at reflux, the reaction does not lead to completion. Moreover, several side-products are formed during the reaction.

In the next step the free amino group was selectively acetylated with acetic anhydride in methanol[33] to afford the N-acetylated derivative. Since not all ester groups were saponified under the conditions applied for the removal of the phthalimido group, the mixture was treated with potassium *tert*-butoxide to give

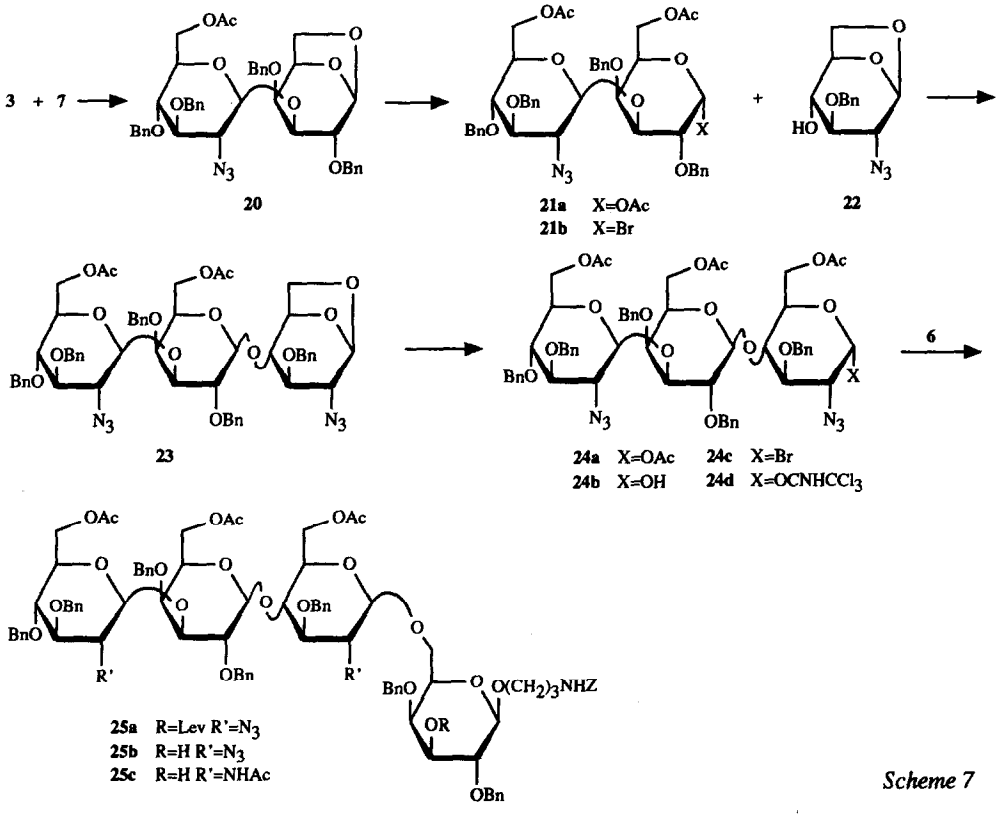
crude **19b**. At this stage, the impure reaction mixture could be successfully purified by reversed phase (RP-18) column chromatography to afford highly pure **19b** in 23 % yield (overall yield from **1**). As an important by-product, compound **19c** was isolated in 20 % yield. Fortunately, this compound, which arises from an incomplete cleavage of the phthalimido group, could be converted into the desired **19b** by subsequent treatment with *n*-butylamine and selective acetylation.

Finally compound **19b** was hydrogenolyzed in the presence of Pd/C in a mixture of *tert*-butanol, water and acetic acid to afford the target pentasaccharide **I**. Since the last reaction proceeded quantitatively it was not necessary to purify the end-product.

SYNTHESIS OF HEPTASACCHARIDE II

Synthesis of glycosyl acceptor 25b

The preparation of the acceptor **25b** for the synthesis of the heptasaccharide is shown in Scheme 7. Thus, glucopyranosyl bromide **7** was coupled with galactose acceptor **3** in the presence of silver silicate-aluminate to give **20** in 70% yield (β/α=5/1). Acetolysis and subsequent treatment with



Scheme 7

titanium tetrabromide provided the disaccharide **21b**, which was coupled in the presence of silver silicate-aluminate with **22** to give only the β-coupled trisaccharide **23** in 54% yield. Opening of the 1,6-anhydro functionality, followed by anomeric saponification gave compound **24b**, which could be converted either into the α-bromide (**24c**)[17] by treatment with the Vilsmeier reagent or into the α-imidate (**24d**) by treatment with trichloroacetonitrile in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU). First, the glycosyl bromide (**24c**) was coupled with the primary hydroxyl group of **6** in the presence of silver silicate-aluminate to give the tetrasaccharide **25a** in a relatively low β/α ratio (β/α=3/1) and in a low yield (34%).

This poor result was not completely unexpected since glycosylation of the same acceptor with the even more reactive monomeric analogue 6-O-acetyl-2-azido-3,4-di-O-benzyl-2-deoxy-α-D-glucopyranosyl bromide (**7**) gave the corresponding disaccharide (**8a**) with a β/α ratio of 4/1 and in a yield of 43%.

As an alternative, the α-imidate donor **24d** was coupled with acceptor **6** in the presence of $BF_3.Et_2O$ to furnish the tetrasaccharide **25a** in 76% yield, but with a less favourable β/α ratio of 2/1. In this case, the coupling with an α-imidate gives a higher yield of the desired β-coupled product than coupling with the corresponding bromide, although the β/α ratio of the latter reaction is lower.

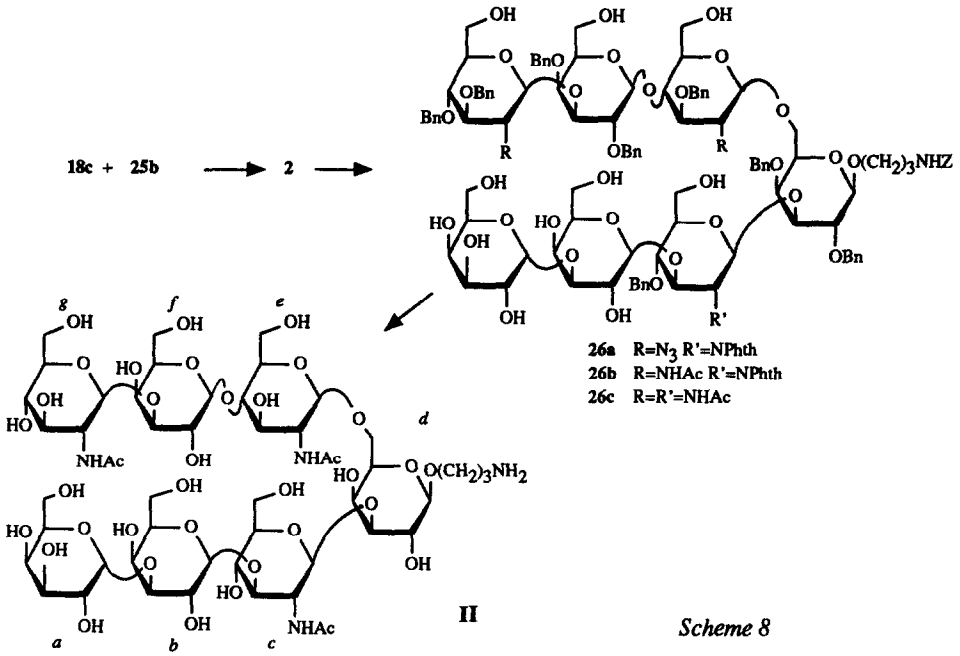
Finally, selective removal of the levulinoyl group with hydrazine acetate provided acceptor **25b**. The corresponding acetylamino derivative **25c** was prepared from **25a** by selective reduction of the azido groups with hydrogen sulphide followed by acetylation of the amino groups and cleavage of the levulinoyl group.

Synthesis of the fully protected heptasaccharide 2 and its deprotection to give II (Scheme 8)

In a first attempt to the synthesis of the protected heptasaccharide **2** (Scheme 2), the glycosyl chloride **18d** was coupled with the tetrasaccharide acceptor **25b** in the presence of AgOTf and 2,6-di-*tert*-butylpyridine. However, only a low yield of the heptasaccharide **2** was obtained. Fortunately, condensation of the glycosyl imidate **18c** with the acceptor **25b** in the presence of a catalytic amount of TMSOTf furnished 60% of the desired β-coupled heptasaccharide **2**. In this respect it is noteworthy that a similar glycosylation in the presence of $BF_3.Et_2O$ as a catalyst gave a very low yield of coupled product.

One of the most important side reactions of this glycosylation was the formation of a product that was also isolated in the synthesis of the pentasaccharide, which probably is a trisaccharide containing an N-trichloroacetyl group at the anomeric centre. Furthermore, glycosylation of a corresponding tetrasaccharide acceptor **25c**, containing two acetylamino groups, with glycosyl imidate **18c** in the presence of TMSOTf also afforded a poor yield of coupled product. The low yield of this reaction might be due to attack of the glycosyl imidate on the acetylamino groups of the acceptor.

Deblocking of the fully protected heptasaccharide **2** was accomplished by the following six-step procedure. First the acetyl and benzoyl esters were cleaved with potassium *tert*-butoxide in a mixture of methanol and dioxane to give compound **26a** in quantitative yield. Selective reduction of the azido groups by hydrogen sulphide treatment in a mixture of pyridine, water and triethylamine, followed by N-acetylation with acetic anhydride in methanol provided the crude compound, which was purified by reversed phase chromatography to give **26b** in 83% yield. In this respect it should be mentioned that



Scheme 8

the reduction of the azido group with hydrogen sulphide proceeds much faster and gives a higher yield when triethylamine is added to the reaction mixture[34]. Under these conditions, however, acyl groups are partly cleaved, which makes it difficult to monitor the reaction on TLC. Therefore, we saponified the acetyl and benzoyl groups before the reduction of the azido groups.

In the next step the phthalimido group was cleaved in the presence of *n*-butylamine and methanol at reflux temperature for 72 hours. Analogously to the deprotection of the pentasaccharide, the mild reagent *n*-butylamine was used in order to avoid cleavage of the benzyloxycarbonyl protective group, but the reaction proceeded sluggishly and also gave rise to the formation of side-products. After selective acetylation of the amino group the crude compound was purified by reversed phase column chromatography to give **26c** in 26% yield.

Finally hydrogenolysis of the benzyl and benzyloxycarbonyl protective groups was conducted in a mixture of *tert*-butanol, water and acetic acid in the presence of palladium on carbon to give **II** in quantitative yield. The structure and identity of **II** were confirmed by NMR spectroscopy. For the assignment of the proton signals, COSY, NOESY and HOHAHA techniques were used.

Conclusion

The results presented in this paper indicate that in oligosaccharide synthesis glycosyl units with non-participating groups at C-2 can not only be used for α-glycosylation but also for β-glycosylation.

The use of 2-azido glycosyl donors for the preparation of β-glycosides has the additional advantage that the deprotection of the azido group proceeds faster and gives a higher yield than the removal of a phthalimido group. On the other hand for the introduction of a β-linkage between two large and unreactive

blocks we still recommend a participating group at C-2 of the donor.

In the synthesis of trisaccharide donor (**18c**), we found that the yield and stereochemical outcome of a coupling reaction are strongly dependent on the leaving group at the anomeric centre and the character of the participating acyl group at C-2. Furthermore we showed that unfavourable steric interaction between the glycosyl donor and the acceptor might strongly influence the α/β ratio of a glycosylation. In this respect the particular conformation of a building block can be of crucial importance for a successful coupling reaction. For instance, we found that the use of the 1,6-anhydro acceptor (**16**) turned out to be essential for an effective synthesis of the described pentasaccharide and the heptasaccharide.

Finally, we demonstrated that pure end-products can be obtained by careful selection of the deprotection conditions and by reversed phase chromatography of the partial deprotected derivatives.

Acknowledgement We wish to thank Mr. G. N. Wagenaars (Organon analytical R&D laboratories) for recording the NMR spectra.

Experimental Part

General procedures

Pyridine was dried by heating with CaH_2 under reflux and then distilled; N,N-dimethylformamide (DMF) was stirred with CaH_2 at room temperature and distilled under reduced pressure. Tetrahydrofuran was distilled from $LiAlH_4$. Dichloromethane, ether and toluene were distilled from P_2O_5. Pyridine was stored over molecular sieves 4Å, toluene and ether over sodium wire and dichloromethane over basic alumina. Reactions were performed under strict anhydrous conditions unless noted otherwise. Optical rotations were recorded at ambient temperature with a Perkin Elmer 241 polarimeter. TLC analysis was performed on Merck-Fertigplatten (Kieselgel 60 F254, 5x10 cm) or on HPTLC Merck-Fertigplatten (Kieselgel 60 F254, 5x5 cm). Compounds were visualized by spraying with sulphuric acid/ethanol (1/4, v/v) or by Usui (110 g of molybdate phosphoric acid dissolved in 2200 ml ethanol and 110 ml sulphuric acid). Normal phase column chromatography was performed on Kieselgel 60, 230-400 Mesh (Merck). Reversed phase column chromatography was performed on LiChroprep RP-18 (40-63 μm) (Merck). ^1H NMR spectra were recorded on a Bruker WM 360 or AM 600 spectrometer equipped with an ASPECT 3000 computer or a Bruker WM 200 spectrometer; chemical shifts are given in ppm (δ) relative to TMS as internal reference, or relative to D_2O.

N-Benzyloxycarbonyl-3-aminopropyl 3,6-di-O-acetyl-2,4-di-O-benzyl-β-D-galactopyranoside (**5a**) - A solution of 3,6-di-O-acetyl-2,4-di-O-benzyl-α-D-galactopyranosyl bromide **4c** (1.01 g, 1.98 mmol) in a mixture of dichloromethane and toluene (4 ml, 2/1) was added at -45 °C to a mixture of 3-N-(benzyloxycarbonylamino)-1-propanol (965 mg, 4.61 mmol), powdered molecular sieves 4Å and silver silicate-aluminate (2.4 g) in dichloromethane (8 ml). After stirring for 2 hours at -45 °C, the mixture was filtered and concentrated to give crude **5a**. Purification on silicagel (dichloromethane/acetone 97/3 → 95/5) afforded **5a** (1.03 g, 82%). R_f 0.49 (dichloromethane/acetone 95/5). ^1H NMR (200 MHz)($CDCl_3$): δ 1.83 (m, 2H, $OCH_2C\underline{H}_2CH_2NHZ$); 1.94, 1.98 (2xs, 6H, 2x$C\underline{H}_3CO$); 3.32 (m, 2H, $OCH_2CH_2C\underline{H}_2NHZ$); 3.55-4.04 (m, 2H, $O\underline{CH}_2CH_2CH_2NHZ$); 3.65 (dt, 1H, H-5, $J_{4,5}$ 1.2 Hz, $J_{5,6}$=$J_{5,6'}$ 6.6 Hz); 3.78 (dd, 1H, H-2, $J_{1,2}$ 7.8 Hz, $J_{2,3}$ 10.3 Hz); 3.86 (dd, 1H, H-4, $J_{3,4}$ 3.1 Hz, $J_{4,5}$ 1.2 Hz); 4.05 (dd, 1H, H-6, $J_{6,6'}$ 11.0 Hz); 4.25 (dd, 1H, H-6'); 4.39 (d, 1H, H-1, $J_{1,2}$ 7.8 Hz); 4.48-5.10 (m, 6H, 3x$OC\underline{H}_2Ph$); 4.78 (dd, 1H, H-3); 7.20-7.40 (m, 15H, H-arom).

N-Benzyloxycarbonyl-3-aminopropyl 2,4-di-O-benzyl-β-D-galactopyranoside (**5b**) - To a solution of compound **5a** (1.03 g, 1.62 mmol) in a mixture of dioxane and methanol (60 ml, 2/1) was added potassium carbonate (485 mg). After stirring for 16 hours at 0 °C, the reaction mixture was neutralized with Dowex 50 (H^+) resin, filtered and concentrated to give **5b** (0.89 g) in quantitative yield. R_f 0.14 (dichloromethane/acetone 9/1).

N-Benzyloxycarbonyl-3-aminopropyl 2,4-di-O-benzyl-6-O-tert-butyldimethylsilyl-β-D-galactopyranoside (**5c**) - *tert*-Butyldimethylsilyl chloride (300 mg, 2.0 mmol) was added to a solution of **5b** (0.89 g, 1.62

mmol) in pyridine (8.5 ml). After stirring for 3½ hours at room temperature, the mixture was concentrated to a small volume. The residue was dissolved in dichloromethane and subsequently washed with water, aqueous $NaHCO_3$ and water. The organic layer was dried and concentrated to give crude **5c** (1.06 g). R_f 0.88 (dichloromethane/acetone 9/1).

*N-Benzyloxycarbonyl-3-aminopropyl 2,4-di-O-benzyl-6-O-tert-butyldimethylsilyl-3-O-levulinoyl-β-D-galactopyranoside (**5d**)* - To a stirred solution of crude **5c** (1.06 g) in pyridine (6.4 ml) was added a solution of levulinic anhydride in tetrahydrofuran (8.0 ml, 0.44 M) and a catalytic amount of 4-dimethylaminopyridine. After stirring for 3¼ hours at room temperature, the mixture was diluted with water and stirring was continued for 30 minutes. Then, dichloromethane was added and the mixture was washed with water. The organic layer was dried and concentrated. The crude product was purified on silicagel (toluene/ethyl acetate 9/1 → 85/15) to give **5d** (1.16 g, 95%). R_f 0.33 (toluene/ethyl acetate 8/2). ^1H NMR (200 MHz)($CDCl_3$): δ 0.04 (s, 6H, $(C\underline{H}_3)_2SiC(CH_3)_3$); 0.88 (s, 9H, $(CH_3)_2SiC(C\underline{H}_3)_3$); 1.87 (m, 2H, $OCH_2C\underline{H}_2CH_2NHZ$); 2.13 (s, 3H, $C\underline{H}_3CO(CH_2)_2CO$); 2.30-2.66 (m, 4H, $CH_3CO(C\underline{H}_2)_2CO$); 3.36 (m, 2H, $OCH_2CH_2C\underline{H}_2NHZ$); 3.79 (dd, 1H, H-2, $J_{1,2}$ 7.8 Hz, $J_{2,3}$ 10.3 Hz); 3.49-4.09 (m, 6H, H-4, H-5, H-6, H-6', $OC\underline{H}_2CH_2CH_2NHZ$); 4.39 (d, 1H, H-1, $J_{1,2}$ 7.8 Hz); 4.94 (dd, 1H, H-3, $J_{2,3}$ 10.3 Hz, $J_{3,4}$ 3.4 Hz); 4.59-5.12 (m, 6H, 3x$C\underline{H}_2$Ph); 7.20-7.40 (m, 15H, H-arom).

*N-Benzyloxycarbonyl-3-aminopropyl 2,4-di-O-benzyl-3-O-levulinoyl-β-D-galactopyranoside (**6**)* - To a solution of **5d** (1.2 g, 1.5 mmol) in tetrahydrofuran (6 ml) was added water (6 ml) and acetic acid (18 ml) and the mixture was stirred for 16 hours at room temperature. The solution was then diluted with dichloromethane and washed with water, aqueous $NaHCO_3$ and water. The organic layer was dried and concentrated to a small volume. Purification of the crude mixture on silicagel (dichloromethane/acetone 9/1 → 1/1) afforded **6** (0.93 g, 95%). R_f 0.36 (dichloromethane/methanol 95/5). ^1H NMR (200 MHz)($CDCl_3$): δ 1.82 (m, 2H, $OCH_2C\underline{H}_2CH_2NHZ$); 2.18 (s, 3H, $C\underline{H}_3CO(CH_2)_2CO$); 2.30-2.90 (c, 4H, $CH_3CO(C\underline{H}_2)_2CO$); 3.34 (m, 2H, $OCH_2CH_2C\underline{H}_2NHZ$); 3.48-4.03 (m, 7H, H-2, -4, H-5, H-6, H-6', $OC\underline{H}_2CH_2CH_2NHZ$); 4.40 (d, 1H, H-1, $J_{1,2}$ 7.9 Hz); 4.92 (dd, 1H, H-3, $J_{2,3}$ 10.3 Hz, $J_{3,4}$ 3.5 Hz); 4.45-5.15 (m, 6H, 3x$C\underline{H}_2$Ph); 7.20-7.40 (m, 15H, H-arom).

*N-Benzyloxycarbonyl-3-aminopropyl 6-O-(6-O-acetyl-2-azido-3,4-di-O-benzyl-2-deoxy-β-D-glucopyranosyl)-2,4-di-O-benzyl-3-O-levulinoyl-β-D-galactopyranoside (**8a**)* - A mixture of compound **6** (92 mg, 0.14 mmol), silver silicate-aluminate (180 mg) and powdered molecular sieves 4Å in dichloromethane (1.3 ml) was stirred at -20 °C. 6-O-Acetyl-2-azido-3,4-di-O-benzyl-2-deoxy-α-D-glucopyranosyl bromide **7** (80 mg, 0.16 mmol) in toluene (0.5 ml) was added dropwise, and the reaction mixture was stirred for 3½ hours at -20 °C. The mixture was diluted with dichloromethane, filtered and the filtrate was concentrated. Purification by chromatography on silicagel (toluene/ethyl acetate 83/17 → 8/2) afforded a mixture of β- and α-coupled disaccharide (80 mg, 53% yield, β/α=4/1). R_f 0.55 (toluene/acetone 8/2). Separation of the β- and α-isomers was performed after removal of the levulinoyl group.

*N-Benzyloxycarbonyl-3-aminopropyl 6-O-(6-O-acetyl-2-azido-3,4-di-O-benzyl-2-deoxy-β-D-glucopyranosyl)-2,4-di-O-benzyl-β-D-galactopyranoside (**8b**)* - To a solution of compound **8a** (together with its α-isomer)(59 mg, 0.056 mmol) in pyridine (0.27 ml) was added a mixture of pyridine (0.27 ml), acetic acid (0.35 ml) and hydrazine monohydrate (0.040 ml). After stirring for 7 minutes at room temperature, the mixture was diluted with dichloromethane. The mixture was washed with water, 1 N HCl, aqueous $NaHCO_3$ and water. The organic layer was dried and concentrated. Purification of the crude product on silicagel (dichloromethane/ethyl acetate 92/8 → 8/2) afforded compound **8b** (41 mg, 76%) and the α-coupled isomer in 19% yield. R_f(**8b**) 0.51 (toluene/acetone 8/2). ^1H NMR (360 MHz)($CDCl_3$) of **8b**: δ 1.83 (m, 2H, $OCH_2C\underline{H}_2CH_2NHZ$); 3.32 (m, 2H, $OCH_2CH_2C\underline{H}_2NHZ$); 3.60-3.70, 3.98-4.06 (2xm, 2H, $OC\underline{H}_2CH_2CH_2NHZ$); 4.51-5.09 (m, 10H, 5x$C\underline{H}_2$Ph); 5.12 (c, 1H, NH); 7.21-7.40 (m, 25H, H-arom).
UNIT *d*: δ 4.36 (d, 1H, H-1, $J_{1,2}$ 7.5 Hz); 3.56 (dd, 1H, H-2, $J_{2,3}$ 9.8 Hz); 3.64 (c, 1H, H-3); 3.77 (dd, 1H, H-4, $J_{3,4}$ 3.5 Hz, $J_{4,5}$ 1.2 Hz).
UNIT *e*: δ 4.33 (c, 1H, H-1); 3.36-3.53 (m, 4H, H-2, H-3, H-4, -5); 4.17 (dd, 1H, H-6, $J_{5,6}$ 4.2 Hz, $J_{6,6'}$ 12.0 Hz); 4.28 (dd, 1H, H-6', $J_{5,6'}$ 1.9 Hz).

*6-O-Acetyl-2,3,4-tri-O-benzyl-α/β-D-galactopyranosyl trichloroacetimidate (**9**)* - To a stirred solution of 6-O-acetyl-2,3,4-tri-O-benzyl-α/β-D-galactopyranoside[35] (4.00 g, 8.13 mmol) in dichloromethane (24 ml) and trichloroacetonitrile (6 ml) was added potassium carbonate (1.92 g). After stirring for 4¼ hours the mixture was filtered and the filtrate was concentrated to give **9** (5.17 g, 100%) as a mixture of α-imidate (13%) and β-imidate (87%). R_f(α) 0.41, R_f(β) 0.48 (dichloromethane/acetone 97/3). ^1H NMR (200 MHz)($CDCl_3$): δ 5.76 (d, H-1(β), $J_{1,2}$ 7.8 Hz); 6.54 (d, H-1(α), $J_{1,2}$ 3.5 Hz).

1,6-Anhydro-2,4-di-O-benzyl-3-O-(6-O-acetyl-2,3,4-tri-O-benzyl-α-D-galactopyranosyl)-β-D-galacto-

*pyranose (**10**)* - To a mixture of glycosyl donor **9** (5.17 g, 8.13 mmol), glycosyl acceptor **3** (2.56, 7.50 mmol) and powdered molecular sieves 4Å in a mixture of ether and dichloromethane (160 ml, 3/1) was added at -45 °C trimethylsilyl trifluoromethanesulfonate (473 µl). After stirring for 75 minutes, solid $NaHCO_3$ was added to the reaction mixture. Next the mixture was filtered and the filtrate was concentrated. Purification on silicagel (toluene/ethyl acetate 94/6 → 9/1) gave **10** (4.29 g, 70%) together with the β-coupled isomer (0.61 g, 10%). $R_f(\alpha)$ 0.56 (toluene/ethyl acetate 8/2); $R_f(\beta)$ 0.61 (toluene/ethyl acetate 8/2). ^1H NMR (360 MHz)($CDCl_3$) of **8**: δ 1.89 (s, 3H, $C\underline{H}_3CO$); 4.15-4.99 (m, 10H, $5xC\underline{H}_2Ph$); 7.15-7.42 (m, 25H, H-arom).
UNIT *a*: δ 5.23 (d, 1H, H-1, $J_{1,2}$ 3.6 Hz); 4.02 (dd, 1H, H-2, $J_{2,3}$ 10.0 Hz); 3.95 (dd, 1H, H-3, $J_{3,4}$ 2.4 Hz); 3.87 (bd, 1H, H-4); 4.16 (m, 1H, H-5); 4.03 (dd, 1H, H-6, $J_{5,6}$ 4.8 Hz, $J_{6,6'}$ 8.0 Hz); 4.12 (dd, 1H, H-6', $J_{5,6'}$ 4.0 Hz).
UNIT *b*: δ 5.29 (t, 1H, H-1, $J_{1,2}=J_{1,3}$ 1.7 Hz); 3.68 (t, 1H, H-2, $J_{1,2}=J_{2,3}$ 1.7 Hz); 4.16 (m, 1H, H-3); 3.90 (m, 1H, H-4); 4.43 (m, 1H, H-5); 3.53 (m, 1H, H-6); 4.56 (m, 1H, H-6').

*1,6-Di-O-acetyl-2,4-di-O-benzyl-3-O-(6-O-acetyl-2,3,4-tri-O-benzyl-α-D-galactopyranosyl)-α/β-D-galactopyranose (**11a**)* - To a solution of compound **10** (3.60 g, 4.41 mmol) in a mixture of acetic anhydride (60 ml) and acetic acid (0.1 ml) was added at 0 °C trifluoroacetic acid (3.5 ml). After stirring for 1 hour at room temperature toluene was added and the mixture was concentrated to give **11a** (3.78 g, 94%). R_f 0.19 (dichloromethane/acetone 98/2).

*6-O-Acetyl-2,4-di-O-benzyl-3-O-(6-O-acetyl-2,3,4-tri-O-benzyl-α-D-galactopyranosyl)-α-D-galactopyranosyl bromide (**11b**)* - To a stirred solution of compound **11a** (139 mg, 0.15 mmol) in a mixture of dichloromethane and ethyl acetate (1.7 ml, 7.5/1) was added at -10 °C a solution of titanium tetrabromide (110 mg, 0.30 mmol) in dichloromethane (1.1 ml). After stirring for 55 minutes at 0 °C toluene was added (15 ml) and dry sodium acetate until the solution became colourless. The mixture was filtered and the filtrate was concentrated to give **11b** (141 mg, 100%). R_f 0.8 (dichloromethane/acetone 97/3). ^1H NMR (200 MHz)($CDCl_3$): δ 1.98, 1.99 (2xs, 6H, $2xC\underline{H}_3CO$); 6.48 (d, 1H, H-1, $J_{1,2}$ 3.7 Hz).

*1,6-Anhydro-2,4-di-O-benzoyl-3-O-(2,3,4,6-tetra-O-benzoyl-α-D-galactopyranosyl)-β-D-galactopyranose (**12**)* - Compound **10** (1.75 g, 2.14 mmol) was dissolved in a mixture of dioxane and methanol (75 ml, 2/1). Potassium carbonate (314 mg) was added and the mixture was stirred for 16 hours at 0 °C. The reaction mixture was then filtered, neutralized with Dowex 50 (H^+) resin, filtered and the filtrate was concentrated. The crude compound was dissolved in ethanol (60 ml) and was treated with hydrogen in the presence of 10% Pd/C (1.32 g). After stirring for 2½ hours the mixture was filtered and the filtrate was concentrated. The debenzylated product was then dissolved in pyridine (60 ml) and benzoyl chloride (2.2 ml) was added. The mixture was stirred for 24 hours where after aqueous $NaHCO_3$ and a catalytic amount of 4-dimethylaminopyridine were added. After stirring for another 15 minutes the mixture was diluted with dichloromethane and washed with water. The organic layer was dried and concentrated. The residue was purified on silicagel (toluene/ethyl acetate 97/3 → 8/2) to give **12** (1.70 g, 84%). R_f 0.34 (toluene/ethyl acetate 9/1). ^1H NMR (360 MHz)($CDCl_3$): δ 7.00-8.15 (m, 30H, H-arom).
UNIT *a*: δ 5.79 (c, 1H, H-1); 5.81 (c, 1H, H-2); 6.11-6.18 (m, 2H, H-3, H-4); 5.04 (m, 1H, H-5); 4.56 (dd, 1H, H-6, $J_{5,6}$ 6.0 Hz, $J_{6,6'}$ 11.2 Hz); 4.63 (dd, 1H, H-6', $J_{5,6'}$ 6.7 Hz).
UNIT *b*: δ 5.50 (t, 1H, H-1, $J_{1,2}=J_{1,3}$ 1.4 Hz); 5.37 (t, 1H, H-2, $J_{1,2}=J_{2,3}$ 1.4 Hz); 4.45 (m, 1H, H-3); 5.44 (bt, 1H, H-4); 4.61 (c, 1H, H-5); 4.68 (d, 1H, H-6, $J_{6,6'}$ 7.5 Hz); 3.80 (m, 1H, H-6').

*1,6-Di-O-acetyl-2,4-di-O-benzoyl-3-O-(2,3,4,6-tetra-O-benzoyl-α-D-galactopyranosyl)-α/β-D-galactopyranose (**13a**)* - To a solution of compound **12** (1.17 g, 1.23 mmol) in acetic anhydride (22.1 ml) and acetic acid (0.2 ml) was added trifluoroacetic acid (3.1 ml). After stirring for 6 hours at 40 °C toluene was added and the mixture was concentrated. The crude compound was purified on silicagel (dichloromethane/acetone 99/1 → 95/5) to give **13a** (1.25 g, 97%). R_f 0.26 (toluene/acetone 9/1).

*6-O-Acetyl-2,4-di-O-benzoyl-3-O-(2,3,4,6-tetra-O-benzoyl-α-D-galactopyranosyl)-α/β-D-galactopyranoside (**13b**)* - A solution of compound **13a** (150 mg, 0.14 mmol) in tetrahydrofuran (1.9 ml) and piperidine (0.13 ml) was stirred for 48 hours at room temperature. Dichloromethane was added and the mixture was subsequently washed with 0.5 N HCl, water, aqueous $NaHCO_3$ and water, dried and concentrated. The residual oil was purified on silicagel (dichloromethane/acetone 97/3 → 9/1) to afford **13b** (127 mg, 88%). R_f 0.17 (dichloromethane/acetone 97/3).

*6-O-Acetyl-2,4-di-O-benzoyl-3-O-(2,3,4,6-tetra-O-benzoyl-α-D-galactopyranosyl)-α-D-galactopyranosyl bromide (**13c**)* - Compound **13a** (669 mg, 0.637 mmol) was dissolved in a mixture of dichloromethane (5.2 ml) and ethyl acetate (0.5 ml) and was cooled to 0 °C. Titanium tetrabromide (702 mg, 1.91 mmol) was added to the stirred solution and stirring was continued for 4 hours at room temperature. The reaction

mixture was then diluted with toluene (30 ml) and dry sodium acetate was added until the mixture became colourless. The mixture was filtered and the filtrate was concentrated to afford **13c** (680 mg, 99%). R_f 0.57 (dichloromethane/acetone 98/2). ^1H NMR (200 MHz)(C_6D_6): δ 1.53 (s, 3H, CH_3CO); 6.49-7.84 (m, 30H, H-arom).
UNIT *a*: δ 6.17 (d, 1H, H-1, $J_{1,2}$ 3.5 Hz); 6.36 (dd, 1H, H-2, $J_{2,3}$ 10.3 Hz); 6.00 (dd, 1H, H-3, $J_{3,4}$ 3.9 Hz); 6.01 (dd, 1H, H-4, $J_{4,5}$ 1.2 Hz).
UNIT *b*: δ 6.15 (dd, 1H, H-2, $J_{1,2}$ 3.8 Hz, $J_{2,3}$ 10.3 Hz); 4.85 (dd, 1H, H-3, $J_{3,4}$ 3.2 Hz); 5.64 (bd, 1H, H-4).

*6-O-Acetyl-2,4-di-O-benzoyl-3-O-(2,3,4,6-tetra-O-benzoyl-α-D-galactopyranosyl)-α-D-galactopyranosyl trichloroacetimidate (***13d***)* - To a solution of **13b** (126 mg, 0.126 mmol) in a mixture of dichloromethane (0.58 ml) and trichloroacetonitrile (0.15 ml) was added potassium carbonate (48 mg). After stirring for 4 hours at room temperature the mixture was filtered and concentrated. The crude compound was chromatographed on silicagel (dichloromethane/acetone 99/1 → 95/5) to give compound **13d** (103 mg, 70%). R_f 0.73 (dichloromethane/acetone 97/3); R ^1H NMR (200 MHz)($CDCl_3$): δ 6.87 (d, 1H, H-1, $J_{1,2}$ 3.8 Hz).

*6-O-Acetyl-2,4-di-O-benzoyl-3-O-(2,3,4,6-tetra-O-benzoyl-α-D-galactopyranosyl)-α-D-galactopyranosyl fluoride (***13e***)* - Compound **13a** (106 mg, 0.101 mmol) was dissolved in dichloromethane (0.25 ml) and cooled to 0 °C. At this temperature 65% HF/pyridine (0.2 ml) was added dropwise to the reaction mixture. After stirring for 16 hours at 0 °C, 0.2 ml 65% HF/pyridine was added and the mixture was stirred for 90 minutes at 10 °C. The reaction mixture was then poured out in aqueous potassium acetate and dichloromethane and stirred for 5 minutes. The organic layer was washed with water, dried and concentrated. The crude product was purified over silicagel (dichloromethane → dichloromethane/acetone 97/3) to afford **13e** (94 mg, 92%). R_f 0.56 (dichloromethane/acetone 97/3). ^1H NMR (200 MHz)($CDCl_3$): δ 6.06 (dd, 1H, H-1, $J_{1,2}$ 2.4 Hz, $J_{1,F}$ 53.5 Hz).

*6-O-Acetyl-2,4-di-O-benzoyl-3-O-(2,3,4,6-tetra-O-benzoyl-α-D-galactopyranosyl)-β-D-galactopyranosyl fluoride (***13f***)* - A solution of **13c** (40 mg, 0.037 mmol) in tetrachloromethane (1.0 ml) and triethylamine tris-hydrofluoride (0.1 ml, 37%) was refluxed for 30 minutes. The reaction mixture was then poured out in aqueous potassium acetate and dichloromethane and stirred for 5 minutes. The organic layer was washed with water, dried and concentrated. Purification of the crude compound was performed on silicagel (toluene/ethyl acetate 9/1 → 8/2) to give **13f** (27 mg, 72%). R_f 0.50 (toluene/ethyl acetate 8/2). ^1H NMR (200 MHz)($CDCl_3$): δ 5.32 (dd, 1H, H-1, $J_{1,2}$ 6.4 Hz, $J_{1,F}$ 52.3 Hz).

*Ethyl 2-deoxy-4,6-O-isopropylidene-2-phthalimido-1-thio-β-D-glucopyranoside (***14a***)* - To a solution of Ethyl 2-deoxy-2-phthalimido-1-thio-β-D-glucopyranose (2.0 g, 5.7 mmol) in N,N-dimethylformamide (10 ml) was added 2,2-dimethoxypropane (4.6 ml, 37.5 mmol) and a catalytic amount of *p*-toluenesulfonic acid monohydrate. After stirring for 20 hours at room temperature, the mixture was poured out in aqueous $NaHCO_3$ and dichloromethane and stirred for 10 minutes. The organic layer was washed with water, dried and concentrated. The crude product was eluted from a silicagel column (toluene/ethyl acetate 1/1) to give **14a** (2.1 g, 93%). R_f 0.64 (toluene/ethyl acetate 1/1). ^1H NMR (200 MHz)($CDCl_3$): δ 1.18 (t, 3H, CH_3CH_2S); 1.42, 1.53 (2xs, 6H, $(CH_3)_2C$); 2.51 (d, 1H, OH, $J_{3,OH}$ 3.5 Hz); 2.67 (m, 2H, CH_3CH_2S); 3.53 (m, 1H, H-5); 3.65 (dd, 1H, H-4, $J_{3,4}$ 8.3 Hz, $J_{4,5}$ 9.5 Hz); 3.82 (dd, 1H, H-6, $J_{5,6}$ 10.0 Hz, $J_{6,6'}$ 10.5 Hz); 4.00 (dd, 1H, H-6', $J_{5,6'}$ 5.4 Hz); 4.27 (t, 1H, H-2, $J_{1,2}$=$J_{2,3}$ 10.3 Hz); 4.48 (m, 1H, H-3); 5.34 (d, 1H, H-1, $J_{1,2}$ 10.3 Hz); 7.68-7.99 (m, 4H, H-arom).

*Ethyl 3-O-[3-O-(2,3,4,6-tetra-O-benzoyl-α-D-galactopyranosyl)-6-O-acetyl-2,4-di-O-benzoyl-α-D-galactopyranosyl]-2-deoxy-4,6-O-isopropylidene-2-phthalimido-1-thio-β-D-glucopyranoside (***15***)* - A mixture of compound **14a** (36 mg, 0.092 mmol), silver trifluoromethanesulfonate (59 mg, 0.23 mmol), 2,6-di-*tert*-butylpyridine (16 µl, 0.073 mmol) and powdered molecular sieves 4Å in dichloromethane (1 ml) was stirred at -50 °C. Glycosyl bromide **13c** (99 mg, 0.092 mmol), dissolved in dichloromethane (0.5 ml), was added dropwise. After stirring for 45 minutes, the reaction mixture was diluted with dichloromethane (5 ml) containing 2,6-di-*tert*-butylpyridine (20 µl) and was filtered. The filtrate was washed with aqueous $NaHCO_3$ and water, dried and concentrated. The crude reaction mixture was eluted from a silicagel column (dichloromethane → dichloromethane/acetone 97/3) to give **15** (29 mg, 23%). R_f 0.44 (dichloromethane/acetone 97/3). ^1H NMR (360 MHz)(C_6D_6): δ 0.95 (t, 3H, CH_3CH_2S); 0.96, 1.36 (2xs, 6H, $(CH_3)_2C$); 1.57 (s, 3H, CH_3CO); 2.41 (m, 2H, CH_3CH_2S); 6.41-8.46 (m, 34H, H-arom).
UNIT *a*: δ 6.03 (, 1H, H-1, $J_{1,2}$ 3.6 Hz); 6.32 (dd, 1H, H-2, $J_{2,3}$ 11.0 Hz); 6.17 (dd, 1H, H-3, $J_{3,4}$ 3.6 Hz); 6.23 (dd, 1H, H-4, $J_{4,5}$ 1.5 Hz); 5.18 (m, 1H, H-5, $J_{5,6}$ 8.0 Hz, $J_{5,6'}$ 6.0 Hz); 4.85 (dd, 1H, H-6, $J_{6,6'}$ 11.2 Hz); 4.94 (dd, 1H, H-6').
UNIT *b*: δ 6.59 (d, 1H, H-1, $J_{1,2}$ 3.5 Hz); 6.03 (dd, 1H, H-2, $J_{2,3}$ 11.3 Hz); 4.91 (dd, 1H, H-3, $J_{3,4}$ 3.0 Hz); 5.71 (dd, 1H, H-4, $J_{4,5}$ 1.3 Hz); 3.97 (m, 1H, H-5, $J_{5,6}$ 6.0 Hz, $J_{5,6'}$ 7.4 Hz); 3.89 (dd, 1H, H-6, $J_{6,6'}$ 10.5

Hz); 4.12 (dd, 1H, H-6').
UNIT *c*: δ 5.61 (d, 1H, H-1, $J_{1,2}$ 10.6 Hz); 4.78 (t, 1H, H-2, $J_{1,2}$=$J_{2,3}$ 10.6 Hz); 5.01 (dd, 1H, H-3, $J_{3,4}$ 8.8 Hz); 3.80 (dd, 1H, H-4, $J_{4,5}$ 9.7 Hz); 3.29 (m, 1H, H-5, $J_{5,6}$ 10.5 Hz, $J_{5,6'}$ 5.5 Hz); 3.47 (t, 1H, H-6, $J_{5,6}$=$J_{6,6'}$ 10.5 Hz); 3.70 (dd, 1H, H-6'). ^{13}C NMR ($CDCl_3$): δ 81.73 (C-1 UNIT *c*); 95.89, 92.70 (C-1 UNIT *a*, C-1 UNIT *b*).

1,6-Anhydro-4-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranose (**16**) - Potassium phthalimide (239 mg, 1.29 mmol) and phthalimide (239 mg, 1.62 mmol) were added to a solution of 1,6:2,3-di-anhydro-4-O-benzyl-β-D-mannopyranose[36] (100 mg, 0.427 mmol) in hexamethylphosphoramide (2.2 ml). After stirring for 20 hours at 170 °C, the reaction mixture was cooled to room temperature. Next the mixture was diluted with ether and subsequently washed with water, 2 N NaOH and water, dried ($MgSO_4$) and concentrated. The crude compound was purified on silicagel (toluene/ethyl acetate 85/15 → 8/2) to give **16** (49 mg, 30%). R_f 0.23 (toluene/ethyl acetate 8/2). ^{1}H NMR (360 MHz)($CDCl_3$): δ 2.18 (d, 1H, OH); 3.43 (dd, 1H, H-4, $J_{3,4}$ 7.6 Hz, $J_{4,5}$ 1.2 Hz); 3.75 (d, 2H, H-6, -6', $J_{5,6}$=$J_{5,6'}$ 3.8 Hz); 4.08 (d, 1H, H-2, $J_{2,3}$ 10.0 Hz); 4.35 (m, 1H, H-3); 4.65 (c, 1H, H-5); 4.71 (AB, 2H, CH_2Ph); 5.57 (s, 1H, H-1); 7.20-7.96 (m, 9H, H-arom).

3-O-[3-O-(2,3,4,6-Tetra-O-benzoyl-α-D-galactopyranosyl)-6-O-acetyl-2,4-di-O-benzoyl-β-D-galactopyranosyl]-1,6-anhydro-4-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranose (**17**) - A solution of compound **16** (241 mg, 0.56 mmol) in dichloromethane (8 ml) containing powdered molecular sieves 4Å was stirred for 30 minutes at room temperature. 2,6-Di-*tert*-butylpyridine (80 µl, 0.36 mmol) and silver trifluoromethanesulfonate (360 mg, 1.40 mmol) were added and the mixture was cooled to -45 °C. A solution of glycosyl bromide **13c** (600 mg, 0.56 mmol) in dichloromethane (4 ml) was added dropwise and stirring was continued for 20 minutes at -45 °C, after which time TLC analysis revealed the formation of one major product. The reaction mixture was poured out in aqueous $NaHCO_3$, diluted with dichloromethane and filtered. The organic layer was washed with water, dried and concentrated. The crude reaction mixture was acetylated in a mixture of pyridine and acetic anhydride (3/1) and a catalytic amount of 4-dimethylaminopyridine. After stirring for 30 minutes toluene was added and the solvents were evaporated. Purification was performed on silicagel (toluene/ethyl acetate 9/1 → 8/2) to give compound **17** (573 mg, 75%). R_f 0.65 (dichloromethane/acetone 95/5). ^{1}H NMR (360 MHz)($CDCl_3$): δ 1.84 (s, 3H, CH_3CO); 4.72-4.81 (2xd, 2H, CH_2Ph); 6.92-8.01 (m, 39H, H-arom).
UNIT *a*: δ 5.66 (d, 1H, H-1, $J_{1,2}$ 3.7 Hz); 5.62 (dd, 1H, H-2, $J_{2,3}$ 10.6 Hz); 5.27 (dd, 1H, H-3, $J_{3,4}$ 3.5 Hz); 4.89 (dd, 1H, H-4, $J_{4,5}$ 1.4 Hz); 3.99 (c, 1H, H-5, $J_{5,6}$ 4.5 Hz, $J_{5,6'}$ 7.8 Hz); 3.71 (dd, 1H, H-6, $J_{6,6'}$ 11.5 Hz); 4.37 (dd,1H, H-6').
UNIT *b*: δ 5.11 (d, 1H, H-1, $J_{1,2}$ 8.0 Hz); 5.54 (dd, 1H, H-2, $J_{2,3}$ 10.1 Hz); 4.12 (dd, 1H, H-3, $J_{3,4}$ 3.5 Hz); 5.61 (bd, 1H, H-4); 3.64 (bt, 1H, H-5); 3.79 (dd, 1H, H-6); 4.03 (dd, 1H, H-6').
UNIT *c*: δ 5.48 (d, 1H, H-1, $J_{1,2}$ 0.5 Hz); 4.31 (dd, 1H, H-2, $J_{2,3}$ 9.6 Hz); 4.60 (dd, 1H, H-3); 3.78 (dd, 1H, H-4, $J_{3,4}$ 6.1 Hz); 3.81 (dd, 1H, H-5, $J_{5,6'}$ 1.6 Hz); 3.79 (d, 1H, H-6, $J_{6,6'}$ 6.0 Hz); 4.64 (dd, 1H, H-6').

3-O-[3-O-(2,3,4,6-Tetra-O-benzoyl-α-D-galactopyranosyl)-6-O-acetyl-2,4-di-O-benzoyl-β-D-galactopyranosyl]-1,6-di-O-acetyl-4-O-benzyl-2-deoxy-2-phthalimido-α/β-D-glucopyranose (**18a**) - To a stirred solution of **17** (570 mg, 0.415 mmol) in acetic anhydride (10 ml) and acetic acid (0.1 ml) was added dropwise at 0 °C trifluoroacetic acid (1.0 ml). After stirring the reaction mixture for 70 minutes at room temperature, toluene was added. The solution was concentrated and twice coevaporated with toluene to give compound **18a** (612 mg, 100%). R_f 0.43 (dichloromethane/acetone 95/5).

3-O-[3-O-(2,3,4,6-Tetra-O-benzoyl-α-D-galactopyranosyl)-6-O-acetyl-2,4-di-O-benzoyl-β-D-galactopyranosyl]-6-O-acetyl-4-O-benzyl-2-deoxy-2-phthalimido-α/β-D-glucopyranose (**18b**) - To compound **18a** (325 mg, 0.221 mmol) was added hydrazine acetate (3.1 ml 0.1 M) in DMF. The mixture was stirred for 2¼ hours at room temperature, after which time it was diluted with dichloromethane and acetic acid. The mixture was washed with water, aqueous $NaHCO_3$ and water, dried and concentrated. Silicagel column chromatography (dichloromethane/acetone 93/7 → 8/2) of the crude product gave **18b** (289 mg, 91%) R_f 0.25 (dichloromethane/acetone 92/8).

3-O-[3-O-(2,3,4,6-Tetra-O-benzoyl-α-D-galactopyranosyl)-6-O-acetyl-2,4-di-O-benzoyl-β-D-galactopyranosyl]-6-O-acetyl-4-O-benzyl-2-deoxy-2-phthalimido-α/β-D-glucopyranosyl trichloroacetimidate (**18c**) - To a stirred solution of **18b** (357 mg, 0.249 mmol) in dichloromethane (1.27 ml) and trichloroacetonitrile (0.33 ml) was added potassium carbonate (104 mg). After stirring for 4½ hours at room temperature the reaction mixture was filtered and the filtrate was concentrated. Column chromatography (toluene/ethyl acetate 7/3 → 1/9) gave **18c** (392 mg, 100 %). R_f 0.60 (toluene/acetone 8/2).

3-O-[3-O-(2,3,4,6-Tetra-O-benzoyl-α-D-galactopyranosyl)-6-O-acetyl-2,4-di-O-benzoyl-β-D-galacto-

pyranosyl]-6-O-acetyl-4-O-benzyl-2-deoxy-2-phthalimido-α/β-D-glucopyranosyl chloride (**18d**) - To a stirred solution of **18b** (60 mg, 0.042 mmol) in a mixture of dichloromethane (0.5 ml) and DMF (0.1 ml) was added a solution of oxalyl chloride in dichloromethane (0.22 ml, 1 M) at 0 °C. After stirring for 50 minutes at room temperature, the reaction mixture was diluted with dichloromethane and washed with cold aqueous $NaHCO_3$ and brine. The organic layer was dried and concentrated to give **18d** (61 mg, 100%) as a mixture of α- and β-chloride. R_f 0.60 (toluene/acetone 8/2). ^1H NMR (200 MHz)($CDCl_3$): δ 5.89 (d, 1H, H-1(β), $J_{1,2}$ 9.6 Hz); 5.99 (d, 1H, H-1(α,) $J_{1,2}$ 3.8 Hz).

Synthesis of the fully protected pentasaccharide (**1**)
A mixture of **18c** (72 mg, 0.046 mmol) and **8b** (42 mg, 0.044 mmol) and pearls molecular sieves 4Å in dichloromethane (1.2 ml) was stirred for 20 minutes at 0 °C. A solution of trimethylsilyl trifluoromethanesulfonate (0.97 µl) in dichloromethane (0.1 ml) was added dropwise to the reaction mixture. After stirring for 2 hours at 0 °C, solid $NaHCO_3$ was added and the mixture was filtered and the filtrate was concentrated. The residue was subsequently chromatographed on Sephadex LH 20 (dichloromethane/methanol 2/1) and on silicagel (dichloromethane/ethyl acetate 9/1 → 7/3) to give **1** (46 mg, 44%).
^1H NMR (600 MHz)($CDCl_3$): δ 1.93, 1.94, 1.98 (3xs, 9H, 3xCH_3CO); 4.20-5.20 (m, 12H, 6xCH_2Ph); 6.81-8.02 (m, 64H, H-arom).
UNIT *a*: δ 5.63 (1H, H-1, $J_{1,2}$ 3.7 Hz); 5.59 (dd, 1H, H-2, $J_{2,3}$ 10.6 Hz); 5.31 (dd, 1H, H-3, $J_{3,4}$ 3.6 Hz); 5.06 (dd, 1H, H-4, $J_{4,5}$ 1.4 Hz); 4.08 (dt, 1H, H-5, $J_{5,6}$=$J_{5,6'}$ 7.2 Hz); 3.84 (dd, 1H, H-6, $J_{6,6'}$ 10.8 Hz); 4.26 (dd, 1H, H-6').
UNIT *b*: δ 4.79 (d, 1H, H-1, $J_{1,2}$ 7.5 Hz); 5.65 (c, 1H, H-2); 3.99 (c, 1H, H-3); 5.56 (dd, 1H, H-4, $J_{3,4}$ 4.5 Hz, $J_{4,5}$ 0.5 Hz); 3.56 (m, 1H, H-5); 3.87 (dd, 1H, H-6, $J_{5,6}$ 7.5 Hz, $J_{6,6'}$ 11.2 Hz); 3.97 (dd, 1H, H-6', $J_{5,6'}$ 7.9 Hz).
UNIT *c*: δ 5.33 (d, 1H, H-1, $J_{1,2}$ 8.5 Hz); 4.35 (dd, 1H, H-2, $J_{2,3}$ 10.6 Hz); 5.06 (dd, 1H, H-3, $J_{3,4}$ 8.2 Hz); 3.75 (dd, 1H, H-4, $J_{4,5}$ 9.9 Hz); 3.69 (m, 1H, H-5); 4.16 (dd, 1H, H-6, $J_{5,6}$ 4.1 Hz, $J_{6,6'}$ 12.0 Hz); 4.44 (dd, 1H, H-6', $J_{5,6'}$ 2.1 Hz).
UNIT *d*: δ 4.28 (d, 1H, H-1, $J_{1,2}$ 8.0 Hz); 3.36 (dd, 1H, H-2, $J_{2,3}$ 10.0 Hz); 3.65 (dd, 1H, H-3, $J_{3,4}$ 3.3 Hz); 3.78 (d, 1H, H-4); 3.54 (dd, 1H, H-5, $J_{5,6}$ 3.8 Hz, $J_{5,6'}$ 8.5 Hz); 3.61 (dd, 1H, H-6, $J_{6,6'}$ 11.0 Hz); 3.68 (dd, 1H, H-6').
UNIT *e*: δ 4.18 (d, 1H, H-1, $J_{1,2}$ 7.8 Hz); 3.36 (dd, 1H, H-2, $J_{2,3}$ 9.0 Hz); 3.31 (t, 1H, H-3, $J_{2,3}$=$J_{3,4}$ 9.0 Hz); 3.45 (bt, 1H, H-4); 3.35 (c, 1H, H-5); 4.16 (c, 1H, H-6); 4.23 (c, 1H, H-6').

Deprotection of pentasaccharide **1**

a) Reduction of the azido group and N-acetylation (**19a**)
Compound **1** (60 mg, 0.025 mmol) was dissolved in a mixture of pyridine and water (2 ml, 5/1). The solution was stirred at room temperature for 2 days and each day hydrogen sulphide was led through the mixture for several hours. TLC analysis indicated conversion of starting material into one major product (R_f 0.25 (toluene/acetone 8/2)). The mixture was neutralized with 1 M acetic acid and evaporated to dryness. The residual oil was coevaporated with pyridine and then dissolved in a mixture of pyridine and acetic anhydride (2 ml, 3/1). After stirring for 30 minutes at room temperature toluene was added and the mixture was concentrated to afford crude **19a**. Gel filtration over Sephadex LH 20 (dichloromethane/methanol 2/1) afforded **19a** (65 mg, crude).

b) Cleavage of the phthalimido group, selective N-acetylation and saponification of the benzoyl and acetyl esters (**19b**)
The crude compound **19a** (65 mg), as obtained in the previous step, was dissolved in a mixture of methanol and *n*-butylamine (4 ml, 5/3) and was refluxed for 96 hours. The reaction mixture was concentrated and dissolved in a mixture of methanol and acetic anhydride (3 ml, 10/1). After stirring for 16 hours at room temperature the mixture was concentrated. The residual oil was dissolved in methanol (0.5 ml) and a catalytic amount of potassium *tert*-butoxide was added. After stirring for 1 hour at room temperature the mixture was neutralized with Dowex 50 (H^+) resin. The resin was filtered off and the filtrate was concentrated to give crude **19b**. The residue was purified by reversed phase chromatography (acetonitrile/water 3/7 → 6/4) to give **19b** (9 mg, 23%, overall from compound **1**) and as a by-product **19c** (8 mg, 20% yield). R_f (**19b**) 0.37 (dichloromethane/methanol 85/15); R_f (**19c**) 0.53 (dichloromethane/methanol 85/15).

c) Hydrogenolysis of the benzyl and benzyloxycarbonyl protective groups. Synthesis of the fully deprotected pentasaccharide **I**
Compound **19b** (6.9 mg, 0.0044 mmol) was dissolved in a mixture of *tert*-butanol (2.1 ml), water (0.5 ml) and acetic acid (0.22 ml) and hydrogenolyzed in the presence of 10% Pd/C (6 mg) for 16 hours. The reaction mixture was filtered and the filtrate was concentrated to give pentasaccharide **I** (4.3 mg, 100%).

$[\alpha]_D$ +49.0 ° (c 0.10, H_2O). FAB(+): 968.3 (MH^+). ^{1}NMR (600 MHz)(D_2O): δ 2.01, 2.04 (2xs, 6H, 2xCH_3CON); 1.97-2.06 (m, 2H, $OCH_2CH_2CH_2NH_2$); 3.17 (m, 2H, $OCH_2CH_2CH_2NH_2$); 3.76-3.84, 3.98-4.04 (m, 2H, $OCH_2CH_2CH_2NH_2$).
UNIT *a*: δ 5.14 (d, 1H, H-1, $J_{1,2}$ 4.0 Hz); 3.85 (dd, 1H, H-2, $J_{2,3}$ 10.4 Hz); 3.95 (dd, 1H, H-3, $J_{3,4}$ 3.4 Hz); 4.01 (d, 1H, H-4); 4.20 (bt, 1H, H-5).
UNIT *b*: δ 4.50 (d, 1H, H-1, $J_{1,2}$ 7.6 Hz); 3.65 (dd, 1H, H-2, $J_{2,3}$ 9.8 Hz); 3.76 (c, 1H, H-3); 4.17 (d, 1H, H-4, $J_{3,4}$ 3.2 Hz).
UNIT *c*: δ 4.74 (d, 1H, H-1, $J_{1,2}$ 8.2 Hz); 3.90 (dd, 1H, H-2); 3.81 (t, 1H, H-3); 3.59 (dd, 1H, H-4, $J_{3,4}$ 8.9 Hz, $J_{4,5}$ 10.0); 3.48 (m, 1H, H-5); 3.78-3.80 (c, 2H, H-6, H-6').
UNIT *d*: 3.39 (d, 1H, H-1, $J_{1,2}$ 7.5 Hz); 3.56 (dd, 1H, H-2); 3.72 (dd, 1H, H-3); 4.13 (d, 1H, H-4, $J_{3,4}$ 3.4 Hz).
UNIT *e*: δ 4.54 (d, 1H, H-1, $J_{1,2}$ 8.3 Hz); 3.71 (c, 1H, H-2); 3.55 (t, 1H, H-3, $J_{2,3}$=$J_{3,4}$ 10.0 Hz); 3.45 (t, 1H, H-4); 3.46 (m, 1H, H-5); 3.76 (c, 1H, H-6); 3.92 (c, 1H, H-6').

*4-O-[3-O-(6-O-Acetyl-2-azido-3,4-di-O-benzyl-2-deoxy-β-D-glucopyranosyl)-6-O-acetyl-2,4-di-O-benzyl-β-D-galactopyranosyl]-6-O-acetyl-2-azido-3-O-benzyl-2-deoxy-α-D-glucopyranosyl trichloroacetimidate (***24d***)* - To a solution of **24b**[17] (916 mg, 0.810 mmol) in dichloromethane (15 ml) was added at -10 °C 1,8-diazabicyclo[5.4.0]undec-7-ene (73 µl) and trichloroacetonitrile (1.65 ml). The mixture was stirred for 45 minutes at -10 °C and for 25 minutes at -5 °C. The reaction mixture was chromatographed on silicagel (toluene/ethyl acetate 8/2 → 1/1) to give **24d** (843 mg, 82%) together with its β-isomer (166 mg, 16%). $R_f(\alpha)$ 0.40 (toluene/ethyl acetate 7/3). ^{1}H NMR of **24d** (200 MHz)($CDCl_3$): δ 6.34 (d, 1H, H-1, $J_{1,2}$ 3.6 Hz); 8.74 (s, 1H, OCNHCCl$_3$).

*N-Benzyloxycarbonyl-3-aminopropyl 6-O-{4-O-[3-O-(6--acetyl-2-azido-3,4-di-O-benzyl-2-deoxy-β-D-glucopyranosyl)-6-O-acetyl-2,4-di-O-benzyl-β-D-galactopyranosyl]-6-O-acetyl-2-azido-3-O-benzyl-2-deoxy-β-D-glucopyranosyl}-2,4-di-O-benzyl-3-O-levulinoyl-β-D-galactopyranoside (***25a***)* - A solution of **24d** (843 mg, 0.661 mmol) and **6** (560 mg, 0.863 mmol) in a mixture of toluene (5.9 ml) and dichloromethane (2.4 ml) containing pearls molecular sieves 4Å was stirred for 20 minutes at room temperature. A solution of boron trifluoride etherate (12.1 µl) in dichloromethane (110 µl) was added at -15 °C. After stirring for 20 minutes the reaction mixture was diluted with dichloromethane and poured out in cold aqueous $NaHCO_3$, washed with brine, dried and concentrated. Column chromatography (hexane/ethyl acetate 3/2 → 1/9) of the residue gave **25a** (606 mg, 51%) and its α-coupled isomer in 25% yield. $R_f(\beta)$ 0.61, $R_f(\alpha)$ 0.59 (toluene/acetone 8/2). ^{1}H NMR of **25a** (360 MHz)($CDCl_3$): δ 1.87-2.16 (4xs, 12H, 4xCH_3CO); 2.27-2.78 (m, 4H, $CH_3CO(CH_2)_2CO$); 4.50-5.10 (m, 16H, 8xCH_2Ph); 7.20-7.43 (m, 40H, H-arom).
UNIT *d*: δ 4.41 (d, 1H, H-1, $J_{1,2}$ 7.6 Hz); 3.76 (dd, 1H, H-2); 4.89 (dd, 1H, H-3, $J_{2,3}$ 9.3 Hz, $J_{3,4}$ 3.4 Hz); 3.85 (d, 1H, H-4); 3.71 (c, 1H, H-5).
UNIT *e*: δ 4.25 (d, 1H, H-1, $J_{1,2}$ 8.0 Hz); 3.34 (dd, 1H, H-2); 3.26 (dd, 1H, H-3).
UNIT *f*: δ 4.29 (d, 1H, H-1, $J_{1,2}$ 7.3 Hz); 3.81 (dd, 1H, H-2); 3.71 (dd, 1H, H-3); 3.82 (d, 1H, H-4, $J_{3,4}$ 2.4 Hz); 3.50 (c, 1H, H-5); 4.02 (c, 1H, H-6); 4.03 (c, 1H, H-6').
UNIT *g*: δ 4.63 (d, 1H, H-1, $J_{1,2}$ 7.9 Hz); 3.37 (c, 1H, H-2); 3.42 (c, 1H, H-3); 3.55 (c, 1H, H-4); 3.46 (c, 1H, H-5); 4.19 (dd, 1H, H-6, $J_{5,6}$ 4.3 Hz, $J_{6,6'}$ 12.2 Hz); 4.44 (dd, 1H, H-6', $J_{5,6'}$ 2.1 Hz).

*N-Benzyloxycarbonyl-3-aminopropyl 6-O-{4-O-[3-O-(6--acetyl-2-azido-3,4-di-O-benzyl-2-deoxy-β-D-glucopyranosyl)-6-O-acetyl-2,4-di-O-benzyl-β-D-galactopyranosyl]-6-O-acetyl-2-azido-3-O-benzyl-2-deoxy-β-D-glucopyranosyl}-2,4-di-O-benzyl-β-D-galactopyranoside (***25b***)* - Compound **25a** (385 mg, 0.218 mmol) was dissolved in a mixture of hydrazine monohydrate (0.16 ml), acetic acid (1.38 ml) and pyridine (2.12 ml) and was subsequently stirred for 7 minutes at room temperature. The reaction mixture was then diluted with dichloromethane and washed with water, 0.5 N HCl, aqueous $NaHCO_3$ and brine, dried and concentrated. The crude product was purified on silicagel (hexane/ethyl acetate 55/45 → 3/7) to afford **25b** (340 mg, 94%). R_f 0.61 (toluene/acetone 8/2).

*N-Benzyloxycarbonyl-3-aminopropyl 6-O-{4-O-[3-O-(6--acetyl-2-acetylamino-3,4-di-O-benzyl-2-deoxy-β-D-glucopyranosyl)-6-O-acetyl-2,4-di-O-benzyl-β-D-galactopyranosyl]-6-O-acetyl-2-acetylamino-3-O-benzyl-2-deoxy-β-D-glucopyranosyl}-2,4-di-O-benzyl-β-D-galactopyranoside (***25c***)* - Compound **25a** (40 mg, 0.023 mmol) was dissolved in a mixture of pyridine (1.2 ml) and water (0.3 ml). Hydrogen sulphide was led through the mixture for 6 hours and the mixture was subsequently stirred for 18 hours. The reaction mixture was neutralized with 1 M acetic acid and evaporated to dryness. The residue was coevaporated with pyridine and then dissolved in pyridine (0.9 ml) and acetic anhydride (0.3 ml). The reaction mixture was stirred for 50 minutes at room temperature. Toluene was added and the mixture was concentrated. The crude product was then treated as described for the synthesis of compound **25b** in order

to cleave the levulinoyl group. Purification of the product was performed on silicagel (dichloromethane/acetone 8/2 → 7/3) to give **25c** (27 mg, 69%). R_f 0.55 (dichloromethane/acetone 7/3). ^{1}H NMR (200 MHz) ($CDCl_3$): δ 1.40, 1.73 (2xs, 6H, 2xCH_3CONH); 1.85, 1.94, 1.97 (3xs, 9H, 3xCH_3COO).

Synthesis of the fully protected heptasaccharide (**2**)
To a solution of compound **18c** (350 mg, 0.222 mmol) and **25b** (137 mg, 0.081 mmol) in dichloromethane (5.0 ml) containing pearls molecular sieves 4Å was added a solution of trimethylsilyl trifluoromethanesulfonate (11 µl) in dichloromethane (0.21 ml) at 0 °C. After stirring for 40 minutes at 0 °C the mixture was diluted with dichloromethane and poured into aqueous $NaHCO_3$. The organic layer was washed with water and brine and then concentrated. The crude product was purified over silicagel (hexane/ethyl acetate 55/45 → 1/9) to afford compound **2** in 60% yield (150 mg). R_f 0.33 (toluene/acetone 8/2). ^{1}H NMR (600 MHz)($CDCl_3$): 1.90-2.02 (5xs, 15H, 5xCH_3CO); 6.80-7.95 (m, 79H, H-arom).
UNIT *a*: δ 5.63 (d, 1H, H-1, $J_{1,2}$ 3.9 Hz); 5.59 (dd, 1H, H-2, $J_{2,3}$ 10.5 Hz); 5.31 (dd, 1H, H-3, $J_{3,4}$ 3.4 Hz); 5.06 (dd, 1H, H-4, $J_{4,5}$ 1.3 Hz); 4.08 (dt, 1H, H-5, $J_{5,6}$=$J_{5,6'}$ 6.5 Hz); 3.81 (c, 1H, H-6); 4.24 (c, 1H, H-6').
UNIT *b*: δ 4.79 (d, 1H, H-1, $J_{1,2}$ 7.4 Hz); 5.65 (c, 1H, H-2); 3.98 (c, 1H, H-3); 5.56 (d, 1H, H-4, $J_{3,4}$ 3.6 Hz); 3.55 (c, 1H, H-5); 3.87 (dd, 1H, H-6); 3.96 (dd, 1H, H-6').
UNIT *c*: δ 5.32 (d, 1H, H-1, $J_{1,2}$ 8.4 Hz); 4.34 (dd, 1H, H-2, $J_{2,3}$ 10.8 Hz); 3.74 (c, 1H, H-4).
UNIT *e*: δ 4.22 (d, 1H, H-1, $J_{1,2}$ 8.1 Hz); 3.31 (dd, 1H, H-2).
UNIT *f*: 4.27 (d, 1H, H-1, $J_{1,2}$ 7.6 Hz); 3.82 (c, 1H, H-2).
UNIT *g*: 4.64 (d, 1H, H-1, $J_{1,2}$ 8.0 Hz); 3.40 (c, 1H, H-2); 3.41 (c, 1H, H-3); 3.55 (c, 1H, H-4); 3.46 (m, 1H, H-5); 4.19 (dd, 1H, H-6); 4.44 (c, 1H, H-6').

Deprotection of heptasaccharide **2**

a) Saponification of benzoyl and acetyl esters (**26a**)
To a solution of **2** (80 mg, 0.026 mmol) in a mixture of dioxane and methanol (8 ml, 1/1,) was added potassium *tert*-butoxide (8 mg). After stirring the mixture for 3¼ hours at room temperature, Dowex 50 (H^+) resin (0.2 g) was added. The resin was filtered off, washed and the filtrate was evaporated to give **26a** in 100% yield (58 mg). R_f 0.40 (dichloromethane/methanol).

b) Reduction of the azido groups and selective N-acetylation (**26b**)
A solution of compound **26a** (58 mg, 0.026 mmol) in a mixture of pyridine, triethylamine and water (4.5 ml, 30/7/8) was treated with hydrogen sulphide for 5 hours. The green solution was neutralized with 1 M acetic acid and evaporated to dryness. The residue was coevaporated with toluene. The crude product was dissolved in a mixture of methanol and acetic anhydride (4.45 ml, 100/15) and the reaction mixture was stirred at room temperature for 16 hours. The solution was concentrated and the residue was purified by reversed phase chromatography (acetonitrile/water 1/1 → 7/3) to give **26b** (49 mg, 83%). R_f 0.58 (dichloromethane/methanol 85/15).

c) Cleavage of the phthalimido group and selective N-acetylation (**26c**)
Compound **26b** (49 mg, 0.022 mmol) was dissolved in a mixture of methanol and *n*-butylamine (2.5 ml, 5/3) and refluxed for 72 hours. The reaction mixture was evaporated to dryness and dissolved in a mixture of methanol and acetic anhydride (2.2 ml, 10/1). The mixture was concentrated and eluted from reversed phase material (acetonitrile/water 4/5 → 65/35) to give **26c** (12 mg, 26% yield). R_f 0.16 (dichloromethane/methanol 85/15).

d) Hydrogenolysis of the benzyl and benzyloxycarbonyl protective groups. Synthesis of the fully deprotected heptasaccharide **II**
To a solution of compound **26c** (12 mg, 0.006 mmol) in a mixture of *tert*-butanol, water and acetic acid (5.25 ml, 14/2/1.5) was added 10% Pd/C (10 mg). The reaction mixture was stirred under hydrogen atmosphere for 16 hours. The catalyst was removed by filtration and the filtrate was concentrated. The material was redissolved in a mixture of *tert*-butanol, water and acetic acid (6.5 ml, 6/6/1) and again hydrogenated for 16 hours in the presence of fresh 10% Pd/C (10 mg). After filtration of the catalyst the mixture was evaporated to dryness to give **II** in quantitative yield (7.5 mg). $[\alpha]_D$ +26.9 ° (c 0.375, H_2O).
FAB(+): 1333.6 (MH^+). ^{1}H NMR (360 MHz)(D_2O): δ 1.98-2.02 (m, 11H, 3xCH_3CO, $OCH_2CH_2CH_2NH_2$); 3.20 (m, 2H, $OCH_2CH_2CH_2NH_2$).
UNIT *a*: δ 5.17 (, 1H, H-1, $J_{1,2}$ 3.9 Hz); 3.89 (dd, 1H, H-2, $J_{2,3}$ 8.5 Hz); 3.98 (dd, 1H, H-3, $J_{3,4}$ 3.5 Hz); 4.04 (d, 1H, H-4); 4.24 (t, 1H, H-5, $J_{5,6}$=$J_{5,6'}$ 8.4 Hz); 3.76 (c, 2H, H-6, H-6').
UNIT *b*: δ 4.54 (, 1H, H-1, $J_{1,2}$ 7.9 Hz); 3.68 (dd, 1H, H-2, $J_{2,3}$ 9.9 Hz); 3.79 (c, 1H, H-3); 4.20 (d, 1H, H-4, $J_{3,4}$ 3.5 Hz).
UNIT *c*: 4.77 (d, 1H, H-1, $J_{1,2}$ 8.4 Hz); 3.93 (dd, 1H, H-2); 3.84 (c, 1H, H-3); 3.62 (t, 1H, H-4, $J_{3,4}$=$J_{4,5}$ 8.4 Hz); 3.51 (c, 1H, H-5); 3.82 (c, 1H, H-6).

UNIT *d*: δ 4.42 (d, 1H, H-1, $J_{1,2}$ 7.9 Hz); 3.59 (c, 1H, H-2); 3.76 (c, 1H, H-3); 4.17 (d, 1H, H-4, $J_{3,4}$ 3.4 Hz).
UNIT *e*: δ 4.59 (d, 1H, H-1, $J_{1,2}$ 7.8 Hz); 3.79 (c, 1H, H-2).
UNIT *f*: δ 4.49 (d, 1H, H-1, $J_{1,2}$ 8.0 Hz); 3.62 (c, 1H, H-2); 3.76 (c, 1H, H-3); 4.19 (d, 1H, H-4, $J_{3,4}$ 3.5 Hz).
UNIT *g*: δ 4.72 (d, 1H, H-1, $J_{1,2}$ 8.3 Hz); 3.79 (c, 1H, H-2); 3.60 (c, 1H, H-3); 3.50 (c, 1H, H-4).

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