# Efficient Preparation of Three Building Blocks for the Synthesis of Heparan Sulfate Fragments: Towards the Combinatorial Synthesis of Oligosaccharides from Hypervariable Regions

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New, multigram routes to suitably protected L-iduronyl monosaccharide donors **4** and **5** and 2-azidoglucose acceptors **6** and **7** are described. The L-iduronyl and D-glucuronyl disaccharides **1**–**3** were then prepared from these compounds, by means of efficient and regioselective protective group manipulations. These disaccharides form the basis of a combinatorial approach toward the synthesis of heparan sulfate fragments representative of the heterogeneous regions of this polysaccharide.

Introduction

## Introduction

Heparan sulfate (HS) is a member of the family of glycosaminoglycans (GAGs). It is a linear, sulfated polysaccharide in which a basic disaccharide, composed of a uronic acid 1−4 linked to a 2-deoxy-2-aminoglucose, is repeated throughout the sequence. HS chains, either at cell surfaces or in the extracellular matrix, interact and regulate the activity of numerous proteins, such as growth factors, cytokines, chemokines, viral proteins, coagulation factors.[1,2] There is growing evidence that the formation of different HS structures is tightly controlled during biosynthesis, with the presumed goal of generating sequences with biological specificity.[3] HS is one of the most heterogeneous biopolymers, since various epimerisation and sulfation patterns (sulfoforms) may occur along the chain.[4−6] The uronic acid may be either D-glucuronic or L-iduronic, while *O*-sulfation may occur on position 2 of the uronic acid and on positions 3 and/or 6 of the amino sugar. The glucosamine nitrogen may be sulfated, acetylated or, less frequently, unmodified (Figure 1), thus resulting in 48 possible disaccharides. From current knowledge of HS biosynthesis, all the theoretical structures cannot be expressed, but 23 of them have already been characterised.[7] The diversity grows exponentially with the polymer length, giving 2304 possible tetrasaccharides, 110,592 hexasaccharides, and more than $5 \cdot 10^6$ octasaccharides.

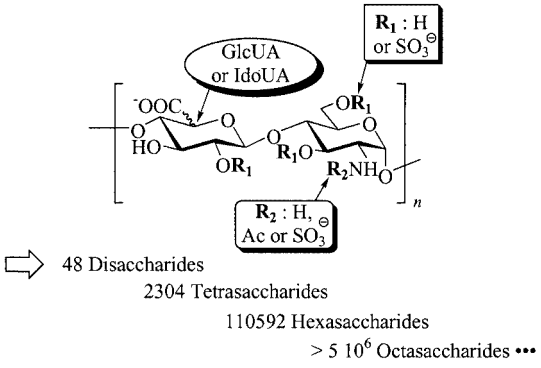


Figure 1. Theoretical molecular diversity found in HS

The polymer, typically composed of 50−200 disaccharide units (25−100 kD), is not fully heterogeneous. Fairly regular *N*-acetylated (NA) regions, mainly composed of glucuronic acid and *N*-acetylated glucosamine, separate hypervariable *N*-sulfated (NS) domains. The latter, typically hexa- to hexadecasaccharides, are expressed dynamically and specifically at the cell surface[3,8] and are responsible for specific interactions with various proteins.[1] New drugs, capable of modulating the activity of a target protein, may emerge from the identification of a HS fragment able to bind selectively and with high affinity to this protein. However, the isolation of NS fragments by enzymatic or chemical degradation of the polymer is impeded by their low level of occurrence. Moreover, HS fragments purified by size ex-

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clusion and ion-exchange chromatography after depolymerisation are often found to be non-homogeneous by PAGE electrophoresis.[9] Total synthesis of HS fragments, although still difficult (in spite of impressive improvements in recent decades[10−16]) is therefore the most efficient way to access structurally defined HS fragments in sufficient amounts for structure-activity studies. Indeed, chemical synthesis has proved to be a valuable tool in the establishment as a drug lead of a pentasaccharide binding to antithrombin and responsible for the anti Xa properties of heparin.[10] This resulted in the development of Arixtra®, an FDA- and EMEA-approved drug against deep vein thrombosis, and of mimetics with enhanced anti IIa properties.[11]

For proteins other than antithrombin, however, the epimerisation and sulfation patterns responsible for the selective binding of a given protein are generally unknown. Synthetic targets are therefore difficult to define, and a combinatorial approach to access the molecular diversity of GAGs seems most appropriate. We have indeed shown, a few years ago, that combinatorial synthesis was an ideal tool with which to generate all the sulfo forms of the basic disaccharides of chondroitin sulfate (another GAG),[17] and since then, developments of building blocks for the modular synthesis of HS fragments have been published by other groups.[18,19] In the meantime, we have started to develop a combinatorial approach for the preparation of HS fragments in order to find compounds able to bind the chemokine SDF-1α selectively and with high affinity.[20] Biochemical studies have shown that the smallest HS fragments to inhibit the interaction between heparin and SDF-1α is an octasaccharide.[21] As shown above, the synthesis of all the HS octasaccharides is unrealistic. However, the SDF-1α binding site on HS chains should be found in the most heterogeneous regions, which are located in the NS or mixed NA/NS domains. We thus decided to restrict the diversity to highly *N*-sulfated octasaccharides, but the diversity would still remain tremendous. We therefore considered the combination of four disaccharides that are of great occurrence in the NS or mixed NA/NS regions: -2-$OSO_3^-$-IdoUA-6-$OSO_3^-$-$GlcNSO_3^-$- (**A**), -2-$OSO_3^-$-IdoUA-$GlcNSO_3^-$- (**B**), -GlcUA-$GlcNSO_3^-$- (**C**), and -GlcUA-GlcNAc- (**D**) (Figure 2). The three building blocks **1**,[22] **2**, and **3** are the precursors of disaccharide domains **A**−**D** and should allow a fully divergent synthesis of HS octasaccharides. Here we report efficient routes to these three building blocks.

The three building blocks **1**−**3** already contain the D-glucuronic or L-iduronic moieties protected as methyl esters in order to avoid oxidation steps that could be troublesome on elaborated material at the end of the synthesis. In order to avoid tedious deprotection schemes, we chose a protective group pattern making clear distinction between the positions to be sulfated and those remaining as free hydroxy groups. Acetates protect the positions to be sulfated, while benzyl ethers are used for permanent protection. A *p*-methoxybenzyl group at the 4′ positions avoids the need to prepare a special building block for capping of the non-reducing end.[23] This group should be removable either together with the benzyl ethers, by hydrogenolysis at the last step of the synthesis, or selectively, by oxidation or acidic treatment, to furnish a disaccharide acceptor for chain elongation. The anomeric positions are protected by an allyl group, which can be removed to give, after activation of the anomeric position, a disaccharide donor. The orthogonality of the *p*-methoxybenzyl and allyl groups can then be used for further elongation of the chain by recurrent deprotection and activation steps.[24]

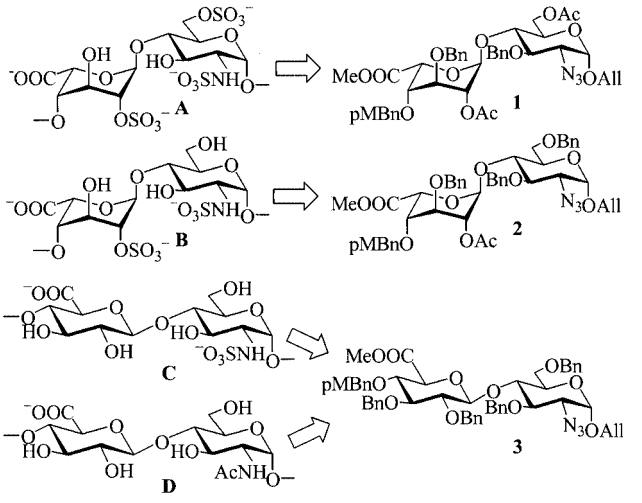



Figure 2. Three disaccharide building blocks for the generation of four HS basic disaccharide

## Results and Discussion

We explored different preparations of the disaccharides **1**−**3** from the restricted number of monosaccharide building blocks **4**−**8** (Figure 3). Since our final goal will require important quantities of disaccharide building blocks, we optimized the preparations of compounds **4**−**7** on multigram scales with the minimum of silica gel chromatography and then followed two strategies for disaccharide preparation. On one hand, monosaccharide building blocks **4** and **6**, containing all the protecting groups in the right position, were condensed to give the disaccharide **1** directly. Donor **4** was prepared from compound **9**, in which an alkenic moiety, used as precursor for the carboxymethyl function, facilitated the introduction of the protecting groups without the limitations often encountered with L-iduronic derivatives, which are prone to β-eliminations, epimerisation, or 2,6-lactone formation. On the other hand, we have also developed the most efficient route so far reported to the less functionalised L-iduronyl donor **5**[25] (72% yield from commercial diacetone glucose). This compound was condensed onto acceptors **6** and **7**, giving disaccharides in which the 4′ positions were differentiated from positions 6 and 2′ by regioselective acetylations. The disaccharide **3**, containing a D-glucuronyl moiety, was prepared in a similar way, by condensation of acetobromoglucose **8**[26] and acceptor **7**,

followed by regioselective protecting group manipulation and oxidation at the 6′ position (Figure 3).

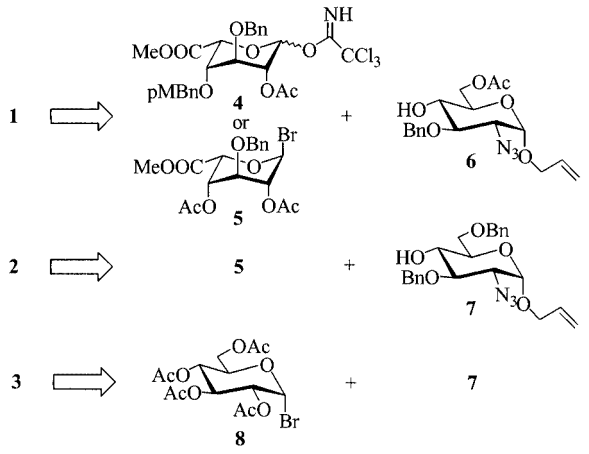


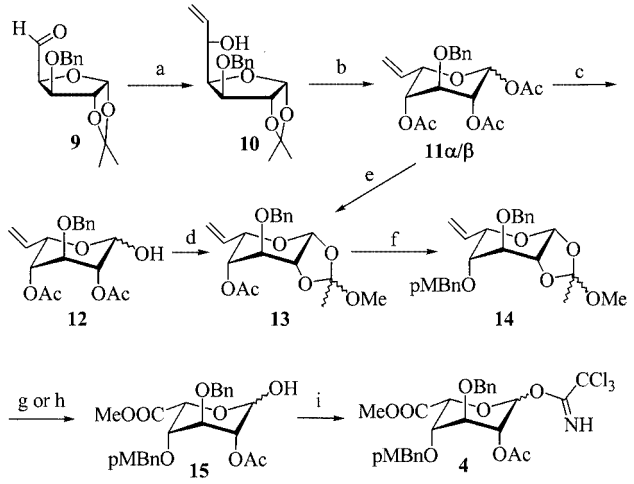
Figure 3. Retrosynthetic analysis for the preparation of the disaccharide building blocks **1**−**3**

### Preparation of the Monosaccharide Building Blocks 4−7

#### Synthesis of Iduronyl Donor 4

We recently showed that the L-idose derivative **10** could easily be prepared from aldehyde **9** by addition of vinylmagnesium bromide (Scheme 1).[27] Compound **10** is an interesting starting material for the synthesis of iduronyl donors, since the alkenic moiety may be efficiently converted into a carboxymethyl group. Moreover, as discussed above, there is no risk of side reactions under basic conditions with such vinylic derivatives, thus facilitating the differentiation of positions 1, 2, and 4. Compound **10** was first converted into the acetylated pyrano derivative **11** by a standard two-step procedure. The 1,2-isopropylidene moiety was cleaved by use of aqueous acetic acid at 80 °C and the resulting triol was acetylated in pyridine with $Ac_2O$, giving 75% of pyrano derivatives **11** together with 25% of furano derivatives (Scheme 1). These were separated by chromatography, and the furano derivatives were recycled by deacetylation and reacetylation, giving a combined yield of 80% for **11α/11β** as a 15:85 mixture. Formation of **11β** as the major anomer is consistent with results obtained previously in the acetylation of **18** and is further supported by NMR spectroscopic data.[28] We then opted for the formation of a 1,2-orthoester to perform the differentiation of position 4 from 1 and 2 (Scheme 1). Our first strategy was based on the preparation of hemiacetal **12** and its conversion into an anomeric halide. Unexpectedly, the selective anomeric deacetylation of **11** proved to be problematic: the classical methods with use of hydrazine acetate[29] or benzylamine[30] resulted in the formation of the expected hemiacetal **12**, which degraded before completion of the reaction with formation of excessively deacetylated product, hydrazone or Schiff base. More unusual methods, such as sodium methoxide in THF[31] or guanidine in methanol,[32] also resulted in the formation of excessively deacetylated compounds. We then turned to the use of lipases as selective deacetylating catalyst, following a methodology successfully used in this laboratory.[33] The α/β mixture **11** was thus treated with Amano AP6 lipase supported on Celite 545 in butan-2-ol, but no conversion could be detected even after prolonged heating at 60 °C. Pig Pancreatic Lipase (PPL), used in phosphate buffer with 10% acetone,[34] proved to be a better catalyst, giving **12** without degradation or excessive deacetylation. Monitoring of the reaction was difficult due to the lack of solubility of **11** and **12** in the aqueous buffer and thus the reaction was not reproducible. To dissolve both compounds, while keeping the PPL catalytically active, we turned to a reverse-micelle emulsion composed of HEPES buffer pH 10, *n*BuOH, octane, and cetyltrimethylammonium bromide (CTAB).[35] Under these conditions, the reaction could easily be followed by TLC, which indicated slow conversion of the β anomer, while transformation of the α anomer was hardly detected. We generally stopped the reaction at around 90% conversion of **11β**. After treatment and purification we obtained **12** (74%), accompanied by a 1:1 α/β mixture of the starting material (25%), which could be recycled (Scheme 1). Hemiacetal **12** was then further converted into the anomeric chloride, by use of Vilsmeier reagent,[36,37] and into the 1,2-orthoester, by use of DMF dimethyl acetal and $Bu_4NBr$,[38] giving **13** in 90% overall yield (Scheme 1). The rate-limiting step in this procedure for the preparation of **13** from **9** is the anomeric deacetylation, which proceeds very slowly (12 days to reach 90% conversion in **11β**). We thus decided to perform a direct conversion of peracetate **11** into an anomeric halide. Classical conditions with HBr in acetic acid, tin or titanium tetrachloride,[39] as well as dichloromethoxymethane/$BF_3{\cdot}Et_2O$,[40] all failed to convert **11** into the corresponding halide, giving mostly decomposition products. Fortunately, the use of TMSBr as brominating agent[41,42] gave the expected anomeric bromide, which was directly converted into the orthoester **13** in a 96% overall yield (Scheme 1). Reactions between TMSBr and peracetylated sugars are generally performed at 80 °C or require the presence of bismuth(III) salts to catalyse the reaction.[43] In the current case, however, the transformation of **11** or its D-*gluco* diastereomer (data not shown) is complete after 2 h at room temp., revealing a greater reactivity of 6-*C*-vinylic derivatives such as **11** with respect to their 6-*O*-acetylated counterparts. The synthesis of **4** was then further completed in a few high-yielding steps. The orthoester **13** was first deacetylated under Zemplén conditions, and the resulting alcohol was alkylated with NaH and *p*-methoxybenzyl bromide, giving orthoester **14** in quantitative yield (Scheme 1). The vinylic moiety in **13** allowed the use of these standard, and high-yielding, alkylation conditions, which, had uronic derivatives been used, would have resulted in β-eliminations and epimerisation. In such a case, alkylation with $Ag_2O$ or under acidic conditions should be used. The latter conditions are incompatible with orthoester protection, while the use of expensive $Ag_2O$ is prohibitive with multigram preparations of building blocks. Compound **14** was then treated with ozone and NaOH in a $CH_2Cl_2$/MeOH mixture



Scheme 1. a) $H_2C{=}CHMgBr$, $Et_2O$, room temp., L-Ido/D-Glc 60:40, 93%; b) i. AcOH/$H_2O$ 7:3, 80 °C; ii. $Ac_2O$, pyridine; 80% after one recycling of the furano derivatives; c) PPL, *n*BuOH/octane/HEPES pH 10, 0.2 M CTAB; 74%; d) i. DMF, $(COCl)_2$, $CH_2Cl_2$; ii. DMF dimethyl acetal, $Bu_4NBr$, $CH_2Cl_2$, reflux; 92%; e) i. TMSBr, $CH_2Cl_2$; ii. DMF dimethyl acetal, $CH_2Cl_2$, reflux; 96%; f) i. MeONa, MeOH; ii. *p*-MeOPhCH$_2$-Br, NaH, DMF; quant; g) i. $O_3$, NaOH, MeOH/$CH_2Cl_2$, −78 °C; ii. AcOH/$H_2O$ 9:1; 73%; h) i. $O_3$, $Me_2S$, $CH_2Cl_2$, −78 °C; ii. *m*CPBA, $H_2O$ pH 7.3; iii. pH 2; iv. $CH_2N_2$; 68%; i) $Cl_3CCN$, $K_2CO_3$, $CH_2Cl_2$; 92%

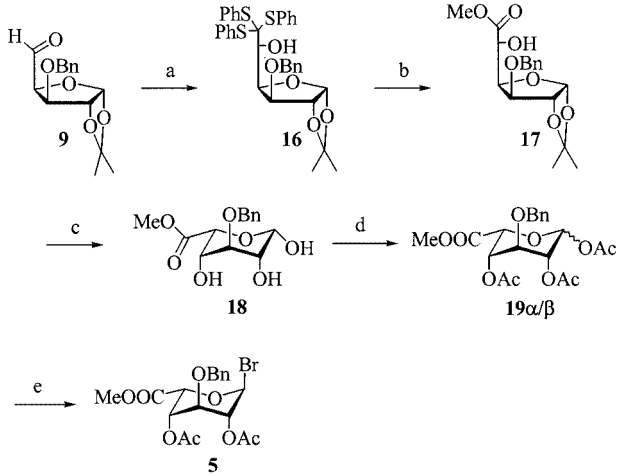
at −78 °C,[44] giving the desired methyl ester with neither β-elimination nor epimerisation. The 1,2-orthoester was opened by use of a 90% aqueous AcOH solution, giving hemiacetal **15** in a 73% overall yield (Scheme 1). Alternatively, ozonolysis followed by a reductive workup with $Me_2S$ was performed on **14**, giving an aldehyde that was oxidized to the corresponding acid with *m*CPBA in aqueous media at pH 7.[27] The 1,2-orthoester was then opened by reduction of the pH to 2, followed by esterification with diazomethane, giving compound **15** in a 68% yield for the four steps. Although this yield is slightly lower than that obtained by the first method, it did establish the use of *m*CPBA in water as an interesting reagent for the oxidation of aldehydes to carboxylic acids, even on highly functionalized molecules.[45] The α/β mixture of hemiacetals **15** was then converted into imidate **4** in 92% yield (Scheme 1). In this reaction, the kinetic β anomer appeared first, followed by the α anomer and further equilibration to a 1:1 ratio. NMR further confirmed this attribution of the α and β configuration.[46] We have thus shown that the synthesis of the iduronyl donor **4**, in eight steps from the vinyl derivative **9**, is efficient (52% global yield) and we have carried it out routinely on 3−4 g scales.

### Synthesis of Iduronyl Donor 5

The approach described above allows the preparation of an iduronyl donor in which all the protecting groups needed in the L-iduronyl moiety of disaccharide building blocks **1** and **2**, are already present. The preparation of the vinylic precursor **9**, however, suffers from low diastereoselectivity. In order to improve the proportion of L-*ido* derivative formed in the addition of organometallic reagent to aldehyde **9**, we have studied the addition of various carboxylate precursors and shown that the addition of tris-phenylthiomethyllithium to **9** exclusively affords the L-*ido* stereoisomer **16** (Scheme 2).[27] This reaction is easily scalable to 100 g and allowed us to devise the most efficient route yet described to the known iduronyl bromide **5**.[25] The trisphenylthioorthoester **16** was treated with $CuO/CuCl_2$[47,48] in a MeOH/$H_2O$/$CH_2Cl_2$ mixture to give the known ester **17**[25] in 94% yield (Scheme 2). This reaction has been scaled up to 39 g with comparable yields. In the earlier synthesis of bromide **5** from **17**,[25] the 1,2-isopropylidene was cleaved quantitatively with trifluoroacetic acid and the resulting mixture was acetylated with $Ac_2O$ in pyridine. Unfortunately, this procedure afforded 40% of furanose derivatives, which had to be separated from the pyrano compounds **19α/β** by tedious chromatography. We have solved this problem by showing that the β-pyrano crystalline form of **18** may be trapped by acetylation if a solvent in which the crystals are only sparingly soluble is used.[49] Thus, on conducting the reaction in dichloromethane at −40 °C, with AcCl as acylating agent, pyridine as base, and DMAP as catalyst, pure **19β** was isolated in 83% yield by simple crystallisation, while 9% additional α/β mixture could be recovered by flash chromatography of the mother liquor (Scheme 2). Thanks to its high isolated yield of pyrano derivatives **19α/β** (92%) and the simplicity of the workup procedure, this procedure is very attractive for large-scale synthesis. Nearly quantitative conversion of **19α/β** into anomeric bromide **5** was then performed with $TiBr_4$, as described.[25] The overall yield of this new synthesis is 72% from commercial diacetone glucose, making this strategy the most attractive route to the useful L-iduronyl synthon **5** yet reported.

### Preparation of 2-Azidoglucosamine Acceptors 6 and 7

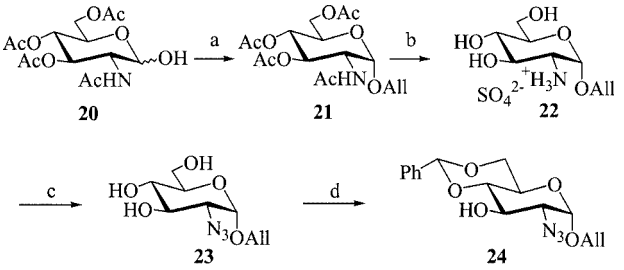
We devised a first access to the acceptors **6** and **7** from α-allyl derivative **21**, which was obtained in 88% isolated



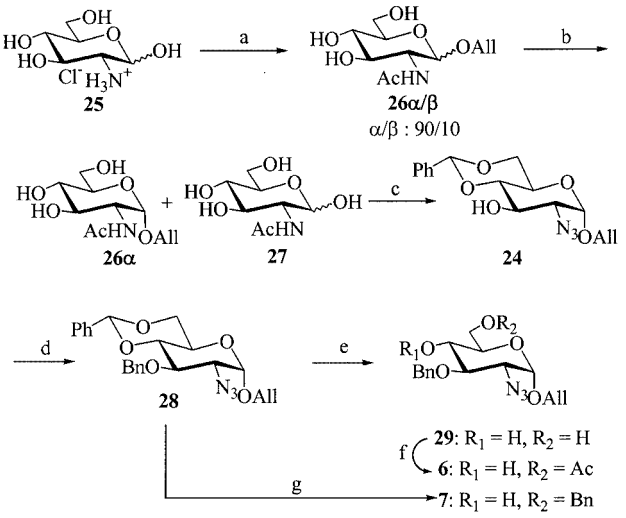
Scheme 2. a) $(PhS)_3CLi$, THF, −78 °C, 92%; b) i. CuO, $CuCl_2$, MeOH/$H_2O$/$CH_2Cl_2$, 94%; c) 9:1 $CF_3COOH/H_2O$ then crystallisation from EtOAc, 80−100%; d) AcCl, pyridine, DMAP, $CH_2Cl_2$, −40 °C, 92%; e) $TiBr_4$, $CH_2Cl_2$, 95%

yield from hemiacetal **20** by α-stereoselective anomeric alkylation[50] (Scheme 3). Compound **21** was *N*- and *O*-deacetylated by heating at reflux with aqueous $Ba(OH)_2$,[51] giving the ammonium salt **22** after neutralisation with aqueous sulfuric acid. Further treatment with the triflyl azide reagent[52,53] gave **23**, which was not isolated at this step, but was converted into the 4,6-*O*-benzylidene derivative **24** in 70% isolated overall yield from **21** (Scheme 3). This first preparation of **24** from **20** is efficient and may be applied on several gram scales. However the synthesis of hemiacetal **20** requires chromatographic purifications, which became unpractical on scales larger than 10 g. We thus turned to a more classical Fischer glycosylation in order to prepare α-allyl glucosaminyl starting material in larger quantities (Scheme 4). The hydrochloride **25** was *N*-acetylated in water and further allylated, as described previously, by use of allyl alcohol and $BF_3{\cdot}Et_2O$.[54,55] This glycosylation is quantitative and may be scaled up to 1 kg.[55] In our hands, unfortunately, the diastereoselectivity of the reaction was only 90:10 in favour of the α anomer **26α**. Moreover, although several later intermediates in the synthesis of **6** and **7** are crystalline, it was impossible to separate the β anomer. We solved this problem by performing a kinetic resolution of the α and β anomers of **26**, taking advantage of the greater reactivity of β anomers toward hydrolysis. Treatment of the **26α/β** mixture with $H^+$ resin in water at 70 °C allowed the total hydrolysis of the β anomer, along with only minor conversion of the α one. The remaining **26α** was then *N*-deacetylated with $Ba(OH)_2$, transformed into the azido derivative **23** as described above, and directly converted into the 4,6-*O*-benzylidene derivative **24**, which was isolated in 50% overall yield from glucosamine hydrochloride **25**. It is worth noting that all the purifications throughout the whole procedure could be performed by use of ion-exchange resins, simple filtration on silica gel pads or crystallisation, which allowed us to carry out this procedure on batches of up to 80 g hydrochloride **25**.[56] Benzylation of compound **24** was then performed quantitatively by standard procedures to give **28**, which can be isolated by simple crystallisation (Scheme 4). Compound **28** was then converted into acceptor **6** in two steps in 95% yield: first transacetalation of the benzylidene moiety in methanol with $H^+$ resin as catalyst, to give the diol **29**, then regioselective acetylation at C-6, with AcCl in pyridine at 0 °C.[57] Alternatively **28** was converted into the benzylated acceptor **7** in 96% yield by a regioselective reductive opening of the 4,6-*O*-benzylidene with HCl in $Et_2O$ and $NaBH_3CN$.[58][59] This reaction can be scaled up to 10 g of **28** with comparable and reproducible yields.




Scheme 3. a) AllBr, NaH, $Bu_4NBr$, $CH_2Cl_2$, −20 °C, 98:2 α/β, 88% isolated α; b) i. $Ba(OH)_2$, $H_2O$, reflux; then neutralisation with $H_2SO_4$; c) $TfN_3$, $CuSO_4$, $CH_2Cl_2$/MeOH/$H_2O$; d) $PhCH(OMe)_2$, TsOH, $CH_3CN$; 70% from **21**



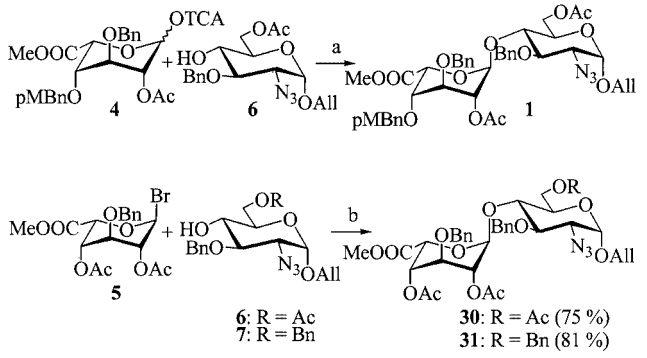

Scheme 4. a) i. $Ac_2O$, $NaHCO_3$, $H_2O$; ii. AllOH, $BF_3{\cdot}Et_2O$, reflux; b) Dowex $H^+$, $H_2O$, 70 °C; c) i. $Ba(OH)_2$, $H_2O$, reflux; then neutralisation with $H_2SO_4$; ii. $TfN_3$, $CuSO_4$, $CH_2Cl_2$/MeOH/$H_2O$; iii. $PhCH(OMe)_2$, TsOH, $CH_3CN$; 50% from glucosamine hydrochloride **25**; d) BnBr, NaH, DMF, 99%; e) Dowex $H^+$, MeOH, 40 °C, 99%; f) AcCl, pyridine, 0 °C; 95%; g) $NaBH_3CN$, HCl, $Et_2O$, 96%

### Preparation of L-Iduronyl Disaccharides 1 and 2

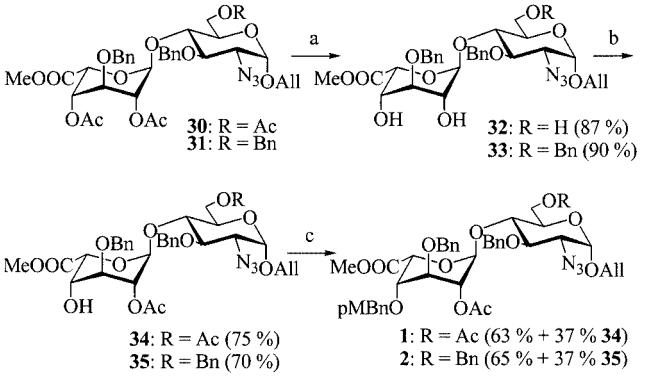
As shown above, the preparations of building blocks **4**−**7** have been optimized on multigram scales. We then studied condensation reactions between the iduronyl donors **4** and **5** and the acceptors **6** and **7** (Scheme 5). The condensation of the fully protected donor **4** onto acceptor **6** was performed in $CH_2Cl_2$ with TMSOTf as a catalyst, giving the target disaccharide building block **1** in 60% yield. The formation of a 1′,2′-*trans* glycoside was confirmed by the measurement of an 1′-H/C′-1 $J^1$ coupling constant of 169 Hz in the non-decoupled $^{13}C$ NMR spectra of disaccharide **1**. Such a value is characteristic of the presence of an equatorial hydrogen at the anomeric position of a pyranose compound, and thus of an α configuration for an L-iduronyl glycoside.[60] In addition, treatment of **1** with DDQ gave disaccharide **34**, in which a hydrogen bond between OH at C′-4 and O′-2 promotes a $^1C_4$ conformation. The $^1H$ NMR spectrum of **34** (Scheme 6) reveals the presence of a $J^4$ W coupling constant of 1.0 Hz between 1′-H and 3′-H, which can only exist if the iduronyl moiety is α linked to the 2-azidoglucose.

Alternatively, coupling of the bromide **5** onto acceptors **6** and **7** in $CH_2Cl_2$ with AgOTf as catalyst gave disaccharides **30** and **31** in 75 and 81% yields, respectively[61] (Scheme 5). Confirmation of the α stereochemistry of the newly created glycosidic linkages was acquired at a later stage in the synthesis. Like compound **1**, disaccharide **30** may be transformed into compound **34** (Scheme 6), the α




Scheme 5. a) TMSOTf, molecular sieves (4 Å), $CH_2Cl_2$, 60%; b) AgOTf, molecular sieves (4 Å), $CH_2Cl_2$, 0 °C, 75% for **30** and 81% for **31**




Scheme 6. a) $K_2CO_3$, MeOH; b) i. $Bu_2SnO$, benzene, reflux; ii. AcCl, $NEt_3$; c) *p*MBnOTCA, $BF_3{\cdot}Et_2O$, −20 °C

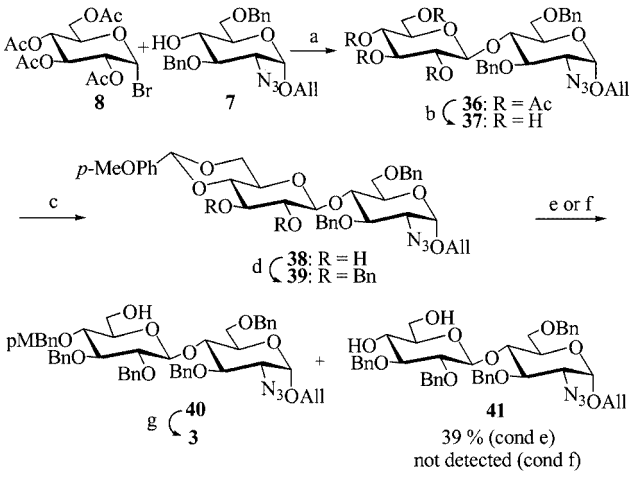
configuration of which was discussed above. The disaccharide **31** may also be converted into disaccharide **35** (Scheme 6), the $^1H$ NMR spectrum of which also revealed the presence of a $J^4$ W coupling constant of 1.0 Hz between 1′-H and 3′-H, indicating an α configuration for the iduronyl moiety. Further transformation of disaccharides **30** and **31** into the disaccharide building blocks **1** and **2** required similar protecting group manipulations (Scheme 6). Both compounds were deacetylated under classical conditions, giving disaccharides **32** and **33** in 90% isolated yields. To differentiate between position 4′ and 2′, we turned to stannylene chemistry.[62][63] Treatment of disaccharide **32** with $Bu_2SnO$ and azeotropic removal of water resulted in the formation of a 2′,4′-stannylene, which allowed 2′-regioselective acylation with AcCl. To perform acetylation of position 6 at the same time, 2.5 equiv. of AcCl were used and $NEt_3$ was added to maintain the pH as slightly basic. Under these conditions, the diacetate **34** was formed as the major product, together with its 4′ regioisomer and triacetylated product. The by-products were deacetylated and reacetylated under the same conditions, giving a combined yield of 75% for **34** (Scheme 6), the $^1H$ NMR spectrum of which confirmed the regioselectivity of the reaction.[64] A similar procedure was used for the selective acetylation of diol **33**, but in this case, only 1.2 equiv. of AcCl and no triethylamine were needed. Under these conditions, the monoacetate **35** was obtained in 70% yield after one recycling step (Scheme 6).[65] The last step in these syntheses is the introduction of the *p*-methoxybenzyl group at the 4′ position, but the presence of an uronic moiety prevented us from performing this alkylation with NaH and *p*-methoxybenzyl bromide. We thus turned to an acid-catalysed alkylation through the use of *p*-methoxybenzyl trichloroacetimidate and $BF_3{\cdot}Et_2O$.[66][67] Although several sets of reaction conditions were studied for this last step, it was not possible to bring the reaction to completion without degradation of the starting material. If, however, the reactions were stopped around 65% conversion, disaccharides **1** and **2** were isolated in 63−65% yields and the unchanged **34** and **35** were recovered nearly quantitatively (Scheme 6). It is worth noting that these incomplete reactions are not a major disadvantage in the perspective of the preparation of longer HS oligosaccharides, since **34** and **35** are disaccharide acceptors for the formation of tetrasaccharides.

### Preparation of Glucuronyl Disaccharide 3

The easily available acetobromoglucose **8** was condensed with acceptor **7** in the presence of AgOTf in $CH_2Cl_2$ at −40 °C, affording the disaccharide **36**, which was deacetylated under Zemplén conditions to give the disaccharide **37** in 80% overall yield (Scheme 7). The deacetylation step, performed directly after extractive workup of the glycosylation reaction, simplified the purifications, through the conversion of the acetobromoglucose into water-soluble derivatives, and allowed us to perform this reaction routinely on 10 g acceptor **7**. As expected, the occurrence of a 7.5 Hz coupling constant between 1′-H and 2′-H in the spectrum of **36** confirmed the formation of a β glycoside. A 4′,6′-*O*-*p*-methoxybenzylidene moiety was then introduced in 89% yield, by use of *p*-anisaldehyde dimethyl acetal and catalytic camphorsulfonic acid, giving disaccharide **38**, which was then benzylated quantitatively to give disaccharide **39** (Scheme 7). A regioselective reductive opening of the 4′,6′-*O*-*p*-methoxybenzylidene was then used as the key step to differentiate position 6′ and 4′. $PhBCl_2$ has recently been introduced as a bulky Lewis acid for the coordination of the C-6 oxygen of a benzylidene ring, to afford, with $Et_3SiH$ as hydride donor, the regioisomer alkylated in the most sterically hindered position.[68] In $CH_2Cl_2$ and with a *p*-methoxybenzylidene group, however, along with the expected **40** (38%), we also obtained the product **41** (39%) resulting from the cleavage of the *p*-methoxybenzylidene group. In order to stabilize reactive charged intermediates, we used a more polar solvent,[69] conducting the reaction in $Et_2O$ at −40 °C. Under these conditions, the disaccharide **40** was obtained in 91% yield (Scheme 7). The regioselectivity of the reductive opening of the *p*-methoxybenzylidene group under this conditions was confirmed by the presence of a triplet, corresponding to an exchangeable proton coupled to 6′-$H^a$ and 6′-$H^b$, in the $^1H$ NMR spectrum of compound **40**. The last step of the synthesis was performed by a two-step methodology that we had already successfully used for the combinatorial preparation of a chondroitin sulfate disaccharide library.[17] The disaccharide **40** was oxid-

ized, by Swern oxidation, to the corresponding aldehyde, which was not isolated. The NMR of the crude mixture after extraction revealed the presence of a single compound with signals corresponding to an aldehyde proton (δ = 8.95 ppm, d, $J$ = 1.5 Hz) and carbon (δ = 196.9 ppm). This product was then directly oxidized to the methyl ester with $I_2$ and methanolic KOH,[17][70] giving disaccharide **3** in 79% yield (Scheme 7). The synthesis of disaccharide building block **3** was thus completed in 54% global yield from acceptor **7** and acetobromoglucose **8**.




Scheme 7. a) AgOTf, molecular sieves (4 Å), $CH_2Cl_2$, −40 °C; b) MeONa, MeOH; 80% from **7**; c) *p*MeOPhCH(OMe)$_2$, TsOH, $CH_3CN$, 89%; d) BnBr, NaH, DMF, 97%; e) $PhBCl_2$, $Et_3SiH$, $CH_2Cl$, −40 °C, 38% of **40** and 39% of **41**; f) $PhBCl_2$, $Et_3SiH$, $Et_2O$, −40 °C, 91% of **40**; g) i. $(COCl)_2$, DMSO, $CH_2Cl_2$, −78 °C; then $NEt_3$, −78 to −20 °C; ii. $I_2$, KOH, MeOH; 79%

## Conclusion

We have designed and developed the preparation of the monosaccharide building blocks **4**−**7** in multigram scale syntheses. These compounds were used to optimize efficient synthesis of disaccharides **1**−**3**, which are essential building blocks for the combinatorial synthesis of HS fragments we are currently developing. In this context, we have already prepared oligosaccharides from the heparin regular region up to the hexadecasaccharide from disaccharide **1**,[24] while oligomerisations of the building blocks **2** and **3** are currently under investigation and will be reported in due course.

## Experimental Section

**General Remarks:** All moisture-sensitive reactions were performed under argon atmospheres in oven-dried glassware. All solvents were dried over standard drying agents[71] and freshly distilled prior to use. Evaporations were performed under reduced pressure. Reactions were monitored by TLC on glass Silica Gel 60 $F_{254}$ plates with detection by UV at 254 nm and by charring with 5% ethanolic $H_2SO_4$. Flash column chromatography was performed on Silica Gel 60 A.C.C. (6−35 μ). Melting points were determined with a Büchi capillary apparatus and are uncorrected. Optical rotations were measured on a Jasco DIP 370 digital polarimeter. NMR spectra were recorded at room temp. with Bruker AC 200, AC 250, AM 250, AM 360, or DRX 400 spectrometers. Chemical shifts δ are given in parts per million (ppm) relative to internal $Me_4Si$ reference, solvent signals ($CDCl_3$ $^{13}C$ δ = 77.0 ppm, [$D_6$]DMSO: $^1H$ δ = 2.49 ppm, $^{13}C$ δ = 39.5 ppm) or acetone in $D_2O$ ($^1H$ δ = 2.225 ppm and $^{13}C$ δ = 30.5 ppm). The allyl group carbons are numbered in the following way: $-O-C^aH_2-C^bH=C^cH_2$, the two protons on C-c were numbered H-cc for the one *cis* to H-b, and H-ct for the one *trans* to H-b. For $^1H$ spectra of iduronyl derivatives, apodisations with Gaussian functions (LB = −1 to −2 Hz and GB = 50%) were used, allowing measurement of coupling constants. COSY, gradient enhanced COSY and HMQC were performed by recording 256 FIDs with 1024 complex data points by use of the standard Bruker programs. Prior to Fourier transformation, the data were zero filled in the $t_1$ dimension to 1024 points and multiplied with a non-shifted sinebell function in both dimensions for COSY; for HMQC, a non-shifted sinebell function in $t_2$ dimension and a non-shifted squared sinebell function in the $t_1$ dimension were used. MS spectra were recorded in the positive mode on a Finnigan MAT 95 S by electrospray ionization. Infrared spectra were recorded on a Fourier transform Bruker IFS66 apparatus. Elemental analyses were performed at the CNRS (Gif sur Yvette, France).

**Large-Scale Preparation of 3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-dialdose (9):** NaH (60% in oil, 13 g, 0.33 mol, 1.65 equiv.) was added in portions to a cooled solution (0 °C) of commercial diacetone glucose (52 g, 0.20 mol) and benzyl bromide (35 mL, 0.30 mol, 1.50 equiv.) in DMF (500 mL). The temperature was then raised to room temp. and the mixture was stirred for 2 h. The temperature was then lowered to 0 °C and the reaction was quenched by addition of *i*PrOH (20 mL), followed by water (400 mL). The resulting solution was extracted with $Et_2O$ (3 × 200 mL) and the combined organic layers were washed with HCl (0.1 M, 2 × 100 mL), water (2 × 100 mL), satd. aqueous $NaHCO_3$ (2 × 100 mL), and then water (2 × 100 mL). The organic phase was filtered through a silicon-treated filter and concentrated. Acetic acid (60 mL) and water (60 mL) were added to the residue and the mixture was stirred for 2 h at 50 °C. The solvents were then evaporated, the remaining traces of acetic acid were removed by coevaporation with toluene, and the residue was purified by chromatography (petroleum ether/EtOAc, 9:1 to 3:7) to give 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose (60.7 g, 98% for the two steps). This compound (0.196 mol) was dissolved in $CH_2Cl_2$ (400 mL), and water (300 mL) was then added, followed by $NaHCO_3$ (5.04 g, 0.03 mol, 0.3 equiv.) and $Bu_4NHSO_4$ (6.7 g, 0.02 mol, 0.1 equiv.). The resulting mixture was cooled (0 °C) and $NaIO_4$ (88 g, 0.4 mol, 2 equiv.) was added in portions over 30 min with vigorous mechanical stirring. The temperature was raised to room temp. and, after 3 h stirring, the mixture was decanted. The aqueous phase was extracted with $CH_2Cl_2$ (3 × 100 mL), the combined organic layers were filtered and concentrated, and the residue was dissolved in 1 L $Et_2O$. The resulting solution was washed with water (4 × 500 mL), dried ($MgSO_4$), filtered, and concentrated, giving **9** (51.7 g, 95%) which was used without further purification. IR (thin film, $cm^{-1}$): $\tilde{\nu}$ = 1735 ($\nu_{C=O}$), 1450, 1372. $^1H$ NMR (250 MHz, $CDCl_3$, ppm): δ = 9.64 (d, $J_{CHO,5}$ = 1.5 Hz, 1 H, C*H*O), 7.24−7.30 (m, 5 H, Ph), 6.11 (d, $J_{1,2}$ = 4.0 Hz, 1 H, 1-H), 4.64 (d, $J_{2,1}$ = 4.0 Hz, 1 H, 2-H), 4.60 (d, $J$ = 12.0 Hz, 1 H, C$H_2$Ph), 4.59 (d, $J$ = 12.0 Hz, 1 H, C$H_2$Ph), 4.50−4.63 (m, 4-H), 4.33 (d, $J_{3,4}$ = 4.0 Hz, 1 H, 3-H), 1.45 and 1.30 (2 s, 2 × 3 H, C$H_3$). $C_{15}H_{18}O_5$ (278.3 g/mol).

**1,2,4-Tri-*O*-acetyl-3-*O*-benzyl-6,7-dideoxy-α,β-L-*ido*-hepta-6-enopyranose (11):** Compound **10**[27,72] (6.30 g, 29.1 mmol) was dissolved in aqueous AcOH (70%, 75 mL), and the solution was heated for 12 h at 80 °C and concentrated. Acetic anhydride (50 mL) was then added to a cooled (0 °C) solution of the residue in pyridine (50 mL). After 16 h stirring at room temp., the mixture was concentrated, residual volatile materials were coevaporated with toluene, and the residue was dissolved in $CH_2Cl_2$ (200 mL). The solution was washed with HCl (0.1 M, 2 × 100 mL), water (2 × 100 mL), satd. aqueous $NaHCO_3$ (2 × 100 mL), and again water (2 × 100 mL). The organic phase was filtered through a silicon-treated filter and concentrated. Flash chromatography of the residue ($CH_2Cl_2$/$Et_2O$, 99:1 to 9:1) gave **11** (7.67 g), as a 15:85 α/β mixture, together with (5*S*)-1,2,5-tri-*O*-acetyl-3-*O*-benzyl-5-*C*-vinyl-L-*arabino*-pentofuranose (2.56 g). A catalytic amount of MeONa was added to a solution of the furano derivatives in MeOH (30 mL). After 2 h at room temp., the reaction mixture was neutralised with Dowex 50X8 200 $H^+$, the resin was filtered off, and the filtrate was concentrated and acetylated as described above, giving another crop of **11** (1.46 g, combined yield 80%). IR (thin film, $cm^{-1}$): $\tilde{\nu}$ = 3297 ($\nu_{C-H,arom.}$), 2098 ($\nu_{C-H,aliph.}$), 1745 ($\nu_{C=O}$), 1663 ($\nu_{C=C}$). $^1H$ NMR of the major β anomer (250 MHz, $CDCl_3$, ppm): δ = 7.43−7.28 (m, 5 H, Ph), 6.14 (d $J_{1,2}$ = 2.0 Hz, 1 H, 1-H), 5.83 (ddd, $J_{6,7t}$ = 17.5, $J_{6,7c}$ = 10.5, $J_{6,5}$ = 6.0 Hz, 1 H, 6-H), 5.38 (dt, $J_{7t,6}$ = 17.5, $J_{gem}$ = $J_{7t,5}$ = 1.5 Hz, 1 H, 7-H$^t$), 5.25 (dt, $J_{7c,6}$ = 10.5, $J_{gem}$ = $J_{7c,5}$ = 1.5 Hz, 1 H, 7-H$^c$), 5.05 (ddd, $J_{2,3}$ = 3.0, $J_{2,1}$ = 2.0, $J_{2,4}$ = 1.0 Hz, 1 H, 2-H), 4.88 (ddd, $J_{4,3}$ = 3.5, $J_{4,5}$ = 2.0, $J_{4,2}$ = 1.0 Hz, 1 H, 4-H), 4.76 (d, $J$ = 12.5 Hz, 1 H, C$H_2$Ph), 4.70 (d, $J$ = 12.5 Hz, 1 H, C$H_2$Ph), 4.65 (ddt, $J_{5,6}$ = 6.0, $J_{5,4}$ = 2.0, $J_{5,7c}$ = $J_{5,7t}$ = 1.5 Hz, 1 H, 5-H), 3.89 (dd, $J_{3,4}$ = 3.5, $J_{3,2}$ = 3.0 Hz, 1 H, 3-H), 2.13, 2.11, 2.06 (3 s, 3 × 3 H, C$H_3$ OAc). $^{13}C$ NMR (62.5 MHz, $CDCl_3$, ppm): δ = 169.9, 169.8, 168.4 (C=O), 136.8 ($C_{quaternary,arom}$), 132.3 (C-6), 128.3, 128.0, 127.6 ($C_{arom}$), 118.5 (C-7), 90.0 (C-1) 74.8, 73.5, 72.8, 68.3, 66.6, 20.7, 20.6 (*C*$H_3$ OAc). $C_{20}H_{24}O_8$ (392.4 g/mol): calcd. C 61.22, H 6.16, O 32.62; found C 61.01, H 6.07, O 32.82.

**2,4-Di-*O*-acetyl-3-*O*-benzyl-6,7-dideoxy-α,β-L-*ido*-Hepta-6-enopyranose (12):** HEPES buffer (50 mM, pH 10, 7.5 mL) was added to a solution of cetyltrimethylammonium bromide (0.2 M, CTAB) in octane/*n*BuOH, 8:2 (492.5 mL). Compound **11** (85:15 α:β mixture, 9.79 g, 24.9 mmol) was dissolved in this reverse-micelle solution (400 mL) with the aid of an ultrasonic bath. An aqueous solution of PPL (250 mg/mL) was added in portions (3 mL) every 12 hours. After 6 days stirring on an orbital shaker, the precipitated enzyme was filtered off with a paper filter and the reaction was allowed to continue for an additional 6 days with periodical addition of PPL solution. The reaction mixture was then filtered through a Celite 545 pad and concentrated. CTAB was precipitated from the residue with acetonitrile and filtered off, and the filtrate was concentrated. Flash chromatography of the residue (toluene/EtOAc, 8:2 to 7:3) gave **12** (6.42 g, 74%) and a 1:1 α:β mixture of **11** (2.42 g, 25%). A major anomer crystallised from $Et_2O$/petroleum (mp = 123−125 °C). IR (thin film, $cm^{-1}$): $\tilde{\nu}$ = 3395, 3194 (3650−3050, $\nu_{O-H}$), 3030, 2982, 2954, 2929 ($\nu_{C-H}$), 1735 ($\nu_{C=O}$), 1455, 1374, 1227, 1158, 1037. $^1H$ NMR (crystalline anomer, 250 MHz, $CDCl_3$, ppm): δ = 7.45−7.25 (m, 5 H, Ph), 5.83 (ddd, $J_{6,7t}$ = 17.0, $J_{6,7c}$ = 10.5, $J_{6,5}$ = 5.5 Hz, 1 H, 6-H), 5.40 (dt, $J_{7t,6}$ = 17.0, $J_{gem}$ = $J_{7t,5}$ = 1.5 Hz, 1 H, 7-H$^t$), 5.25 (dt, $J_{7c,6}$ = 10.5, $J_{gem}$ = $J_{7c,5}$ = 1.5 Hz, 1 H, 7-H$^c$), 5.20 (dd, $J_{1,OH}$ = 10.0, $J_{1,2}$ = 1.5 Hz, 1 H, 1-H), 4.92−4.83 (m, 2 H, 2-H, 4-H), 4.76 (d, $J$ = 12.0 Hz, 1 H, C$H_2$Ph), 4.70 (d, $J$ = 12.0 Hz, 1 H, C$H_2$Ph), 4.54 (dq, $J_{5,6}$ = 5.5, $J_{5,4}$ = $J_{5,7c}$ = $J_{5,7t}$ = 1.5 Hz, 1 H, 5-H), 3.91 (t, $J_{3,4}$ = $J_{3,2}$ = 3.0 Hz, 1 H, 3-H), 3.44 (d, $J_{OH,1}$ = 10.0 Hz, OH), 2.22, 2.02 (2 s, 2 × 3 H, C$H_3$ OAc). $^{13}C$ NMR (62.5 MHz, $CDCl_3$, ppm): δ = 170.3, 170.0 (C=O), 137.0 ($C_{quaternary,arom}$), 132.9 (C-6), 128.3, 128.0, 127.5 ($C_{arom}$), 117.8 (C-7), 91.6 (C-1), 73.8, 73.3, 72.7 (*C*$H_2$ Bn), 68.1, 20.7, 20.6 (*C*$H_3$ OAc). $C_{18}H_{22}O_7$ (350.4 g/mol): calcd. C 61.71, H 6.33, O 31.96; found C 61.72, H 6.41, O 32.18.

**4-*O*-Acetyl-3-*O*-benzyl-6,7-dideoxy-1,2-(1-methoxyethylidene)-β-L-*ido*-hepta-6-enopyranose (13). Synthesis from Hemiacetal 12:** DMF (2.6 mL, 32 mmol, 3.0 equiv.) was added to a solution of compound **12** (3.90 g, 11.1 mmol) in $CH_2Cl_2$ (100 mL), followed by oxalyl chloride (9.7 mL, 111 mmol, 10 equiv.). After 14 h stirring at room temp., the solution was poured into a mixture of $Et_2O$ (500 mL), satd. aqueous $NaHCO_3$ (300 mL), and crushed ice (100 g), and the aqueous phase was quickly extracted with ice-cold $Et_2O$ (100 mL). The combined organic phases were washed with ice-cold water (2 × 100 mL), dried ($MgSO_4$), filtered, concentrated, and the residual water was coevaporated with toluene. DMF dimethyl acetal (7.3 mL, 55 mmol, 5 equiv.) and $Bu_4NBr$ (3.6 g, 11.1 mmol, 1 equiv.) were then added to a solution of the resulting chloride in $CH_2Cl_2$ (100 mL). After 20 h at reflux, the reaction mixture was diluted with $Et_2O$ (500 mL), washed successively with satd. aqueous $NaHCO_3$ (200 mL) and water (2 × 200 mL), dried ($MgSO_4$), filtered, and concentrated. The residue was generally used directly in the next step, but could be purified by flash chromatography of the residue (petroleum ether/EtOAc, 95:5 to 85:15, 0.5% $NEt_3$) to give **13** (3.65 g, 90%) as one stereoisomer (presumably *exo*). $^1H$ NMR (200 MHz, $CDCl_3$, ppm): δ = 7.45−7.30 (m, 5 H, Ph), 5.80 (ddd, $J_{6,7t}$ = 17.5, $J_{6,7c}$ = 10.5, $J_{6,5}$ = 5.5 Hz, 1 H, 6-H), 5.55 (d, $J_{1,2}$ = 3.0 Hz, 1 H, 1-H), 5.37 (dt, $J_{7t,6}$ = 17.5, $J_{gem}$ = $J_{7t,5}$ = 1.5 Hz, 1 H, 7-H$^t$), 5.24 (dt, $J_{7c,6}$ = 10.5, $J_{gem}$ = $J_{7c,5}$ = 1.5 Hz, 1 H, 7-H$^c$), 4.84 (dt, $J_{4,3}$ = 3.0, $J_{4,5}$ = $J_{4,2}$ = 1.5 Hz, 1 H, 4-H), 4.78 (d, $J$ = 12.0 Hz, 1 H, C$H_2$Ph), 4.66 (d, $J$ = 12.0 Hz, 1 H, C$H_2$Ph), 4.40 (dq, $J_{5,6}$ = 5.5, $J_{5,4}$ = $J_{5,7c}$ = $J_{5,7t}$ = 1.5 Hz, 1 H, 5-H), 4.08 (ddd, $J_{2,1}$ = 3.0, $J_{2,3}$ = 2.0, $J_{2,4}$ = 1.5 Hz, 1 H, 2-H), 4.04 (dd, $J_{3,4}$ = 3.0, $J_{3,2}$ = 2.0 Hz, 1 H, 3-H), 3.26 (s, 3 H, C$H_3$ OMe), 2.05 (s, 3 H, C$H_3$ OAc), 1.73 (s, 3 H, C$H_3$ orthoester). $^{13}C$ NMR (62.5 MHz, $CDCl_3$, ppm): δ = 170.6 (C=O), 133.5 (C-6), 132.0 ($C_{quaternary,arom}$), 128.6, 128.2, 127.8 ($C_{arom}$), 123.8 (C quat. orthoester), 117.7 (C-7), 96.5 (C-1), 76.2, 72.8, 72.2, 67.7, 49.0, (*C*$H_3$ OMe), 25.1 (*C*$H_3$ orthoester), 20.8 (*C*$H_3$ OAc). $C_{19}H_{24}O_7$ (364.4 g/mol).

**Synthesis from Peracetate 11:** TMSBr (13 mL, 111 mmol, 5 equiv.) was added to a cooled (0 °C) solution of compound **11** (8.5 g, 22.1 mmol) in $CH_2Cl_2$ (75 mL). After the mixture had been stirred for 2 h at room temp., the solvent and excess reagent were evaporated. DMF dimethyl acetal (14.8 mL, 111 mmol, 5 equiv.) was then added to a solution of the crude bromide in $CH_2Cl_2$ (200 mL). The reaction mixture was heated at reflux for 12 hours, treated as above and used directly in the next step.

**3-*O*-Benzyl-6,7-dideoxy-4-*O*-(4-methoxybenzyl)-1,2-(1-methoxyethylidene)-β-L-*ido*-hepta-6-enopyranose (14):** MeONa (60 mg, 0.57 mmol, 0.4 equiv.) was added to a solution of crude **13**, obtained from **12** (1 g, 2.85 mmol), in methanol (10 mL). After 20 h stirring at room temp., the reaction mixture was concentrated, and the residual methanol was azeotropically removed with toluene. NaH (60% in oil, 240 mg, 6 mmol, 2.1 equiv.) was added to a cooled (0 °C) solution of the residue in DMF (10 mL). After the mixture had been stirred for 5 min at 0 °C, *p*MeOBnBr (1.04 g, 5.2 mmol, 1.8 equiv.) was added and the reaction mixture was stirred for one hour at room temp. It was then quenched with *i*PrOH (1 mL), followed by water (10 mL), and diluted with $Et_2O$ (100 mL). The organic phase was washed with water (3 × 50 mL), dried ($MgSO_4$), filtered, and concentrated. Flash chromatography

of the residue (petroleum ether/EtOAc, 9:1 to 8:2, $NEt_3$ 0.5%) gave **14** (1.16 g, 92%) as one stereoisomer (presumably *exo*).

***Note:*** *p*MeOBnBr was prepared from *p*MeOBnOH (750 μL, 6 mmol) by treatment with HBr (33% in AcOH, 7.5 mL). After 30 min at room temp., the mixture was concentrated, and the residue was diluted with toluene (50 mL), washed with satd. aqueous $NaHCO_3$ (10 mL) and water (10 mL), filtered through a silica gel pad eluted with toluene, and concentrated to give *p*MeOBnBr (1.04 g, 84%).

**Data for 14:** $[\alpha]_D^{30} = -31$ (*c* = 1.0, toluene). IR (thin film, $cm^{-1}$): $\tilde{\nu}$ = 3063, 3027 ($\nu_{C-H,arom.}$), 2998, 2940, 2911, 2836 ($\nu_{C-H,aliph.}$), 1612, 1586, 1514, 1455, 1431, 1384, 1317, 1303, 1250, 1208, 1173, 1152. $^1H$ NMR (250 MHz, $CDCl_3$, ppm): δ = 7.40−7.25 (m, 5 H, Ph), 7.21 (d, *J* = 8.5 Hz, 2 H, *Ph*-OMe), 6.84 (d, *J* = 8.5 Hz, 2 H, *Ph*-OMe), 5.96 (ddd, $J_{6,7t}$ = 17.0, $J_{6,7c}$ = 10.5, $J_{6,5}$ = 6.0 Hz, 1 H, 6-H), 5.52 (d, $J_{1,2}$ = 3.0 Hz, 1 H, 1-H), 5.35 (dt, $J_{7t,6}$ = 17.0, $J_{gem}$ = $J_{7t,5}$ = 1.5 Hz, 1 H, 7-H$^t$), 5.23 (dt, $J_{7c,6}$ = 10.5, $J_{gem}$ = $J_{7c,5}$ = 1.5 Hz, 1 H, 7-H$^c$), 4.61 (d, *J* = 11.5 Hz, 1 H, C$H_2$Ph), 4.55 (d, *J* = 11.5 Hz, 1 H, C$H_2$Ph), 4.53 (d, *J* = 11.5 Hz, 1 H, C$H_2$PhOMe), 4.38 (d, *J* = 11.5 Hz, 1 H, C$H_2$PhOMe), 4.24 (dq, $J_{5,6}$ = 6.0, $J_{5,4}$ = $J_{5,7c}$ = $J_{5,7t}$ = 1.5 Hz, 1 H, 5-H), 4.13 (ddd, $J_{2,1}$ = 3.0, $J_{2,3}$ = 2.0, $J_{2,4}$ = 1.0 Hz, 1 H, 2-H), 4.05 (dd, $J_{3,4}$ = 3.0, $J_{3,2}$ = 2.0 Hz, 1 H, 3-H), 3.80 (s, 3 H, C$H_3$ OMe *p*MBn), 3.34 (ddd, $J_{4,3}$ = 3.0, $J_{4,5}$ = 1.5, $J_{4,2}$ = 1.0 Hz, 1 H, 4-H), 3.28 (s, 3 H, C$H_3$ OMe orthoester), 1.68 (s, 3 H, C$H_3$ orthoester). $^{13}C$ NMR (62.5 MHz, $CDCl_3$, ppm): δ = 159.1 (*C*-OMe, *p*MBn), 137.3 ($C_{quaternary,arom}$), 134.7 (C-6), 130.0, 129.1, 128.5, 128.0, 127.7 ($C_{arom}$), 123.8 (C quat. orthoester), 117.1 (C-7), 113.5 ($C_m$ *p*MBn), 96.7 (C-1), 76.5, 73.8, 72.5, 72.4 (*C*$H_2$ Bn or *p*MBn), 72.1, 71.5 (*C*$H_2$ Bn or *p*MBn), 55.1 (*C*$H_3$ Ph-OMe), 48.9, (*C*$H_3$ OMe orthoester), 25.0 (*C*$H_3$ orthoester). $C_{25}H_{30}O_7$ (442.5 g/mol): calcd. C 67.86, H 6.83; found C 68.11, H 6.92.

**Methyl 2-*O*-Acetyl-3-*O*-benzyl-4-*O*-(4-methoxybenzyl)-L-idopyranuronate (15):** Ozone was bubbled through a cooled (−78 °C) solution of orthoester **14** (2.7 g, 6.1 mmol) in a mixture of $CH_2Cl_2$ (170 mL) and methanolic NaOH (2.5 M, 50 mL, 125 mmol, 20 equiv.).[44] The solution turned dark orange, which slowly faded and turned to typical ozone blue after 4 h. TLC (toluene/EtOAc, 9:1, $R_{f\mathbf{14}}$ = 0.60) indicated that the intermediate aldehyde ($R_f$ = 0.33) was formed first, followed by the ester ($R_{f\mathbf{15}}$ = 0.45). Ozone was bubbled through the solution until completion of the reaction. A mixture of aqueous $KH_2PO_4$ solution (1 M, 115 mL), satd. aqueous $NaHCO_3$ solution (20 mL) and satd. aqueous $Na_2S_2O_3$ solution (50 mL) was then poured onto the cold (−78 °C) reaction mixture. After warming to room temp., the aqueous phase was extracted with EtOAc (3 × 200 mL). The combined organic phases were filtered through a silicon-treated filter and concentrated. The resulting oil was dissolved in aqueous AcOH (90%, 150 mL) and the reaction mixture was stirred for 45 min at room temp. and concentrated. Flash chromatography of the residue (toluene/EtOAc, 75:25 to 60:40) gave **15** (2.06 g, 73%). Data for the 60:40 α/β mixture: $^1H$ NMR (250 MHz, $CDCl_3$, ppm): δ = 7.43−7.25 (m, 5 H, Ph), 7.07 and 7.04 (d, *J* = 8.5 Hz, 2 H, *Ph*-OMe), 6.81 and 6.80 (d, *J* = 8.5 Hz, 2 H, *Ph*-OMe), 5.33 (dt, $J_{1,OH}$ = 9.0, $J_{1,2}$ = $J_{1,3}$ = 1.5 Hz, 0.6 H, H-1α), 5.12 (dd, $J_{1,OH}$ = 11.5, $J_{1,2}$ = 2.0 Hz, 0.4 H, H-1β), 4.86 (d, $J_{5,4}$ = 3.0 Hz, 0.6 H, H-5α), 4.82−4.78 (m, 1 H, 2-H α and β), 4.71 (d, *J* = 11.5 Hz, 0.6 H, C$H_2$Ph), 4.68 (d, *J* = 11.5 Hz, 0.4 H, C$H_2$Ph), 4.63 (d, *J* = 11.5 Hz, 0.6 H, C$H_2$Ph), 4.58 (d, *J* = 11.5 Hz, 0.4 H, C$H_2$Ph), 4.57 (d, $J_{5,4}$ = 2.0 Hz, 0.4 H, H-5β), 4.37 (d, *J* = 11.0 Hz, 0.6 H, C$H_2$PhOMe), 4.33 (d, *J* = 11.5 Hz, 0.4 H, C$H_2$PhOMe), 4.32 (d, *J* = 11.0 Hz, 0.6 H, C$H_2$PhOMe), 4.27 (d, *J* = 11.5 Hz, 0.4 H, C$H_2$PhOMe), 4.18 (d, $J_{OH,1}$ = 9.0 Hz, 0.6 H, OH α), 3.98 (t, $J_{3,2}$ = $J_{3,4}$ = 3.5 Hz, 0.4 H, H-3β), 3.90 (td, $J_{3,2}$ = $J_{3,4}$ = 4.0, $J_{3,1}$ = 1.5 Hz, 0.6 H, H-3α), 3.87−3.70 (m, 7.4 H, including 2 s at δ = 3.79 and 3.74: 2 × C$H_3$ OMe), 2.03 (s, 1.2 H, C$H_3$ OAc), 2.00 (s, 1.8 H, C$H_3$ OAc). $^{13}C$ NMR (62.5 MHz, $CDCl_3$, ppm): δ = 170.8, 170.4, 169.8, 169.2 (C=O), 159.1 (*C*-OMe, *p*MBn), 137.0, 136.7 ($C_{quaternary,arom}$), 134.4, 129.6, 129.5, 129.2, 129.1, 128.9, 128.5, 128.4, 128.2, 128.1, 128.0, 127.9 ($C_{arom}$), 113.5 ($C_m$ *p*MBn), 93.1/91.8 (C-1), 74.1, 73.2, 72.9/72.5 (*C*$H_2$ Bn or *p*MBn), 72.1 (*C*$H_2$ Bn or *p*MBn), 71.4, 71.2, 68.4, 67.9, 55.1 (*C*$H_3$, Ph-OMe), 52.2/52.1 (*C*$H_3$, COOMe), 20.9 (*C*$H_3$ OAc). $C_{24}H_{28}O_9$ (460.5 g/mol): calcd. C 62.60, H 6.13, O 31.21; found C 62.01, H 6.26, O 30.61.

**Alternative Preparation of 15 by Ozonolysis and Oxidation of the Intermediate Aldehyde with *m*CPBA in Water:** Ozone was bubbled through a cooled (−78 °C) solution of orthoester **14** (177 mg, 0.4 mmol) in $CH_2Cl_2$ (4 mL) until the colour tuned to a permanent blue. The excess ozone was then eliminated by bubbling argon, and dimethyl sulfide (300 μL, 4 mmol, 10 equiv.) was added. The temperature was raised to room temp. over 3 h and the solvent was evaporated. *m*CPBA (200 mg, 0.8 mmol, 2 equiv.) was then added to a suspension of the residue in phosphate buffer (pH, 7.3, 1 M, 7 mL). After two hours under vigorous stirring, the reaction was quenched with an aqueous $Na_2S_2O_3$ solution (1 M, 800 μL) and the pH was lowered to 2 by careful addition of aqueous $H_2SO_4$ (1 M). The mixture was stirred for 15 min at room temp. and then extracted with EtOAc (3 × 5 mL). The combined organic layers were filtered through a silicon-treated filter and concentrated. A freshly prepared ethereal solution of diazomethane (6 mL) was added to a solution of the residue in $Et_2O$ (2 mL). After destruction of the excess diazomethane with AcOH, the solvent was evaporated and the residue was purified as described above, giving **15** (126 mg, 68%).

**Methyl 2-*O*-Acetyl-3-*O*-benzyl-4-*O*-(4-methoxybenzyl)-α,β-L-idopyranuronate Trichloroacetimidate (4):** Trichloroacetonitrile (4.0 mL, 41 mmol, 6.0 equiv.) and $K_2CO_3$ (1.67 g, 13.6 mmol, 2.0 equiv.) were added to a solution of compound **15** (3.13 g, 6.9 mmol) in $CH_2Cl_2$ (12 mL). TLC (toluene/acetone, 8:2) showed that the β anomer ($R_f$ = 0.73) appeared first, followed by the α anomer ($R_f$ = 0.63). After 6 h stirring at room temp. the reaction mixture was directly applied to the top of a flash chromatography column and eluted (toluene/EtOAc, 95:5 to 8:2, 0.1% $NEt_3$), giving **4** (3.85 g, 92%) as a 1:1 α/β mixture. Data for the α anomer: $^1H$ NMR (250 MHz, $CDCl_3$, ppm): δ = 8.64 (s, 1 H, N*H*), 7.42−7.27 (m, 5 H, Ph), 7.10 (d, *J* = 8.5 Hz, 2 H, *Ph*-OMe), 6.82 (d, *J* = 8.5 Hz, 2 H, *Ph*-OMe), 6.40 (t, $J_{1,2}$ = $J_{1,3}$ = 1.3 Hz, 1 H, 1-H), 5.11 (dt, $J_{2,3}$ = 3.0, $J_{2,1}$ = $J_{2,4}$ = 1.3 Hz, 1 H, 2-H), 4.94 (d, *J* = 2.5 Hz, 1 H, 5-H), 4.74 (d, *J* = 12.0 Hz, 1 H, C$H_2$Ph), 4.57 (d, *J* = 12.0 Hz, 1 H, C$H_2$Ph), 4.45 (d, *J* = 11.5 Hz, 1 H, C$H_2$PhOMe), 4.36 (d, *J* = 11.5 Hz, 1 H, C$H_2$PhOMe), 3.90 (ddd, $J_{3,4}$ = 3.5, $J_{3,2}$ = 3.0, $J_{3,1}$ = 1.3 Hz, 1 H, 3-H), 3.81 (ddd, $J_{4,3}$ = 3.5, $J_{4,5}$ = 2.5, $J_{4,2}$ = 1.3 Hz, 1 H, 4-H), 3.79 (s, 3 H, C$H_3$ OMe), 3.73 (s, 3 H, C$H_3$ OMe), 2.06 (s, 3 H, C$H_3$ OAc). $^{13}C$ NMR (62.5 MHz, $CDCl_3$, ppm): δ = 169.8, 169.0 (*C*=O), 160.0 (*C*=NH), 159.3 (*C*-OMe, *p*MBn), 137.2 ($C_{quaternary,arom}$), 130.1, 128.3, 127.8, 127.7 ($C_{arom}$), 113.6 ($C_m$ *p*MBn), 95.3 (C-1), 94.3 (*C*$Cl_3$), 73.0, 72.0 (2 × C), 70.2, 69.7, 65.3, 55.1 (*C*$H_3$ OMe *p*MBn), 52.2 (*C*$H_3$ OMe ester), 20.8 (*C*$H_3$ OAc). Data for the β anomer: $^1H$ NMR (250 MHz, $CDCl_3$, ppm): δ = 8.66 (s, 1 H, N*H*), 7.43−7.28 (m, 5 H, Ph), 7.08 (d, *J* = 8.5 Hz, 2 H, *Ph*-OMe), 6.81 (d, *J* = 8.5 Hz, 2 H, *Ph*-OMe), 6.20 (d, $J_{1,2}$ = 2.0 Hz, 1 H, 1-H), 5.22 (ddd, $J_{2,3}$ = 3.5, $J_{2,1}$ = 2.0, $J_{2,4}$ = 1.0 Hz, 1 H, 2-H), 4.69 (d, *J* = 12.0 Hz, 1 H, C$H_2$Ph), 4.67 (d, $J_{5,4}$ = 2.5 Hz, 1 H, 5-H), 4.59 (d, *J* = 12.0 Hz, 1 H, C$H_2$Ph), 4.41 (d, *J* = 11.5 Hz, 1 H, C$H_2$PhOMe), 4.33 (d, *J* = 11.5 Hz, 1 H,

C$H_2$PhOMe), 3.95 (t, $J_{3,2} = J_{3,4} = 3.5$, 1 H, 3-H), 3.81−3.75 (m including s at δ = 3.78, 4 H, 4-H and C$H_3$ OMe), 3.72 (s, 3 H, C$H_3$ OMe), 2.05 (s, 3 H, C$H_3$ OAc). $^{13}$C NMR (62.5 MHz, $CDCl_3$, ppm): δ = 170.5, 168.0 (*C*=O), 160.3 (*C*=NH), 159.3 (*C*-OMe, *p*MBn), 136.8 ($C_{quaternary,arom}$), 129.5, 128.4, 128.1, 127.9 ($C_{arom}$), 113.6 ($C_m$ *p*MBn), 94.2 (C-1), 90.4 (*C*$Cl_3$), 74.8, 73.0, 72.6, 72.2, 71.8, 65.7, 55.1 (*C*$H_3$, Ph-OMe), 52.2 (*C*$H_3$, COOMe), 20.8 (*C*$H_3$ OAc). $C_{26}H_{28}Cl_3NO$ (604.9 g/mol).

**Tris(thiophenyl) 3-*O*-Benzyl-1,2-*O*-isopropylidene-β-L-orthoidofuranuronate (16):** *n*BuLi (195 mL of a 1.2 M soln. in hexane, 0.274 mol, 1.2 equiv.) was added to a cooled (−78 °C), mechanically stirred solution of tris(thiophenyl)methane (93.2 g, 0.274 mol, 1.3 equiv.) in THF (400 mL). Upon addition of *n*BuLi the colour changed to bright yellow and a yellow solid then precipitated. After the mixture had been stirred for 1.5 h at this temperature, a solution of **9** (57 g, 0.205 mol) in THF (400 mL) was added dropwise. The mixture was stirred for 1 h at the same temperature and was then allowed to come to room temp. overnight. Satd. aqueous $NH_4Cl$ (500 mL) was then added, and the aqueous phase was extracted with $Et_2O$ (3 × 400 mL). The combined organic layers were washed with water (2*100 mL), dried ($MgSO_4$), filtered, and concentrated. Flash chromatography of the residue (petroleum ether/EtOAc, 9:1 to 8:2) gave **16** (116.7 g, 92%) the $^1$H and $^{13}$C data for which were identical to those previously reported.[27] $C_{34}H_{34}O_7S_3$ (618.8 g/mol).

**Methyl 3-*O*-Benzyl-1,2-*O*-isopropylidene-β-L-idofuranuronate (17):** Methanol (1.33 L), CuO (8.53 g, 106.6 mmol, 1.7 equiv.), $CuCl_2$ (32.0 g, 237.0 mmol, 3.8 equiv.), and water (115 mL) were successively added to a solution of compound **16** (38.9 g, 63.4 mmol) in $CH_2Cl_2$ (115 mL). The reaction mixture was vigorously shaken for 2 h, filtered through a Celite 545 pad and concentrated without warming above 30 °C. The residue was dissolved in $CH_2Cl_2$ (1 L), and water (500 mL) was added, giving a Cu salt precipitate that was eliminated by filtration through a Celite 545 pad. After decantation, the aqueous layer was extracted with $CH_2Cl_2$ (2 × 250 mL). The combined organic layers were washed with a satd. aqueous $NaHCO_3$ solution (200 mL) and water (200 mL), filtered through a silicon-treated filter, and concentrated. Flash chromatography of the residue (toluene followed by petroleum ether/EtOAc, 7:3 to 1:1) gave **17** (19 g, 89%), the $^1$H and $^{13}$C NMR spectra of which were identical to those previously reported.[25] $C_{17}H_{22}O_7$ (338.4 g/mol).

**Methyl 3-*O*-Benzyl-L-idofuranuronate (18):** Compound **17** (15.4 g, 45.5 mmol) was dissolved in a mixture of trifluoroacetic acid (85.5 mL) and water (9.5 mL). After 20 min stirring at room temp., the solvents were evaporated and the resulting solution was coevaporated with water (3 × 30 mL). The residue was crystallised from EtOAc, to which the minimum pyridine necessary to reach neutrality has been added, giving a quantitative yield of **18** (13.5 g), the analytical data for which were identical to those described previously.[25] $C_{14}H_{18}O_7$ (298.3 g/mol).

**Methyl 1,2,4-Tri-*O*-acetyl-3-*O*-benzyl-α,β-L-idofuranuronate (19):** 2,4-Dimethylaminopyridine (172 mg, 1.4 mmol, 0.1 equiv.), pyridine (11.3 mL, 141 mmol, 10 equiv.) and acetyl chloride (6 mL, 84.6 mmol, 6 equiv.) were added to a cooled (−40 °C) suspension of crystalline **18** (4.2 g, 14.1 mmol) in $CH_2Cl_2$ (70 mL). After 10 h stirring at this temperature, the mixture was diluted with dichloromethane (200 mL) and the resulting organic phase was washed with saturated $NaHCO_3$ solution (3 × 50 mL), water (2 × 50 mL), $H_2SO_4$ (1 M, 3 × 50 mL), and water (3 × 50 mL), filtered through a phase separator filter, and concentrated. The residue was crystallised from $Et_2O$, giving **19β** (5.0 g, 11.7 mmol, 83%). Evaporation of the mother liquor followed by flash chromatography gave additional **19α/β** (1:2) mixture (0.5 g, combined yield in **19α/β**: 92%). $C_{18}H_{21}BrO_8$ (424.4 g/mol).

**Methyl 2,4-Di-*O*-acetyl-3-*O*-benzyl-L-idofuranuronyl Bromide (5):** $TiBr_4$ (4.4 g, 12.1 mmol, 1.28 equiv.) was added to a solution of **19** (4 g, 9.43 mmol) in $CH_2Cl_2$ (90 mL). The resulting mixture was stirred for 5 h at room temp., diluted with $CH_2Cl_2$ (100 mL), and washed with ice-cold water (100 mL). The organic layer was filtered through a Celite 545 pad, and the filtrate was filtered through a phase silicon-treated filter and concentrated, giving **5** (3.95 g), the analytical data for which were identical to those described previously.[25] This compound was used without further purification. $C_{20}H_{24}O_{10}$ (445.3 g/mol).

**Allyl 2-Azido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (24):** Acetic anhydride (10.4 mL, 0.11 mol, 1.1 equiv.) was added dropwise to a solution of glucosamine hydrochloride **25** (21.6 g, 0.1 mol) and $NaHCO_3$ (20.2 g, 0.24 mol, 2.4 equiv.) in water (250 mL). After 90 min at room temp., the mixture was concentrated to 50 mL, passed through a Dowex 50X8 200 $H^+$ column (500 mL) and collected into a batch of Dowex IX8 200 $HCO_3^-$ (500 mL). The resin was filtered off, the solution was concentrated, and the residue was dried over $P_2O_5$ at 40 °C under vacuum, giving a quantitative yield of *N*-acetyl-glucosamine. Allyl alcohol (250 mL, 3.7 mol, 37 equiv.) and $BF_3{\cdot}Et_2O$ (3.7 mL, 25 mmol, 0.25 equiv.) were successively added to the crude *N*-acetyl-glucosamine, and the mixture was heated at reflux overnight.[54,55] The solution was then concentrated and dried over $P_2O_5$, giving a quantitative yield of **26α/β** as an 90:10 α/β mixture. $^{13}$C NMR (62.9 MHz, $D_2O$, ppm): δ = 174.6 (C=O), 133.9 (C-b α), 133.6 (C-b β), 118.3 (C-c β), 118.1 (C-c α), 100.3 (C-1 β), 96.3 (C-1 α), 76.1 (β), 74.1 (β), 72.1, 71.2, 70.6 (β), 70.2, 68.6, 61.0, 60.8, 55.7 (C-2 β), 53.9 (C-2 α), 22.4 (*C*$H_3$, NHAc β), 22.1 (*C*$H_3$, NHAc α). $C_{11}H_{19}NO_6$ (488.2 g/mol).

Dowex 50X8 200 $H^+$ (11 g) was added to a solution of crude **26α/β** in water (100 mL), and the mixture was heated at 70 °C. The hydrolysis of the β anomer was followed by $^{13}$C NMR with reference to the β anomeric carbon signal at δ = 100.1 ppm and was complete after 15 h at 70 °C. The mixture was cooled to room temp., the resin was filtered off, and the filtrate was neutralised with Dowex IX8 200 $HCO_3^-$. The resin was filtered off and the filtrate was concentrated to 400 mL, $Ba(OH)_2{\cdot}8H_2O$ (56.8 g, 0.18 mol, 1.8 equiv.) was then added, and the mixture was heated at reflux overnight.[51] The brown solution was cooled to 0 °C and neutralised with sulfuric acid (3 M), and the precipitated barium sulfate was removed by centrifugation. The collected supernatant was concentrated, giving crude **22** as a brown oil. $^1$H NMR(250 MHz, $D_2O$, ppm): δ = 5.99 (dddd, $J_{b,ct} = 17.0$, $J_{b,cc} = 10.5$, $J_{b,a'} = 6.0$, $J_{b,a} = 5.0$ Hz, 1 H, H-b), 5.37 (dq, $J_{ct,b} = 17.0$, $J_{ct,a} = J_{ct,a'} = J_{gem} = 1.5$ Hz, 1 H, H-ct), 5.27 (dq, $J_{cc,b} = 10.5$, $J_{cc,a} = J_{cc,a'} = J_{gem} = 1.5$ Hz, 1 H, H-cc), 4.92 (d, $J_{1,}2 = 3.5$ Hz, 1 H, 1-H), 4.24 (ddt, $J_{gem} = 13.0$, $J_{a,b} = 5.0$, $J_{a,cc} = J_{a,ct} = 1.5$ Hz, 1 H, H-a), 4.05 (ddt, $J_{gem} = 13.0$, $J_{a',b} = 6.0$, $J_{a',cc} = J_{a',ct} = 1.5$ Hz, 1 H, H-a′), 3.90−3.65 (m, 3 H, 5-H, 6-H$^a$, 6-H$^b$), 3.55 (dd, $J_{3,2} = 10.0$, $J_{3,4} = 9.5$ Hz, 1 H, 3-H), 3.38 (t, $J_{4,3} = J_{4,5} = 9.5$ Hz, 1 H, 4-H), 2.72 (dd, $J_{2,3} = 10.0$, $J_{2,1} = 3.5$ Hz, 1 H, 2-H).

A solution of triflyl azide in $CH_2Cl_2$ was prepared as described,[52,53] from $NaN_3$ (65 g, 1 mol) and triflic anhydride (36 mL, 0.21 mol) [***Caution:*** $TfN_3$ is reported to be explosive when dry]. This solution was added dropwise, over 50 min, to a cooled (0 °C) solution of crude **22**, $K_2CO_3$ (20.7 g, 0.15 mol) and $CuSO_4$ (160 mg, 1 mmol) in water (100 mL) and MeOH (150 mL). MeOH (up to 250 mL) was added during the addition to keep the system

monophasic. The reaction mixture was then stirred overnight at room temp. and $BuNH_2$ (30 mL, 0.30 mol) was added. After three hours stirring, the reaction mixture was adsorbed on silica gel (70−200 μ, 130 mL) and filtered through a silica gel pad (600 mL, EtOAc/MeOH, 98:2 to 50:50). The solvents were evaporated, the residue was eluted with water from a Dowex 50X8 200 $H^+$ column (500 mL), and the fractions containing **23** were neutralised with Dowex IX8 200 $HCO_3^-$. The resin was filtered off and the water was evaporated, giving crude allyl 2-azido-2-deoxy-α-D-glucopyranoside **23** (15.0 g). For purposes of characterisation, a small amount of **23** was purified by flash chromatography ($CH_2Cl_2$/MeOH, 9:1 to 8:2). $[\alpha]_D^{29} = -124$ ($c$ = 1.0, MeOH). IR (thin film, $cm^{-1}$): $\tilde{\nu}$ = 3329 (3700−3000, $\nu_{O-H}$), 2924 (3750−3000, $\nu_{C-H}$), 2099 ($\nu_{N3}$), 1647, 1454, 1421, 1337. $^1H$ NMR (250 MHz, $D_2O$, ppm): δ = 5.98 (dddd, $J_{b,ct}$ = 17.5, $J_{b,cc}$ = 10.5, $J_{b,a'}$ = 6.0, $J_{b,a}$ = 5.0 Hz, 1 H, H-b), 5.39 (dq, $J_{ct,b}$ = 17.5, $J_{ct,a}$ = $J_{ct,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-ct), 5.29 (dq, $J_{cc,b}$ = 10.5, $J_{cc,a}$ = $J_{cc,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-cc), 5.10 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.24 (ddt, $J_{gem}$ = 12.5, $J_{b,a}$ = 5.0, $J_{cc,a}$ = $J_{ct,a}$ = 1.5 Hz, 1 H, H-a), 4.09 (ddt, $J_{gem}$ = 12.5, $J_{b,a'}$ = 6.0, $J_{cc,a'}$ = $J_{ct,a'}$ = 1.5 Hz, 1 H, H-a′), 3.91−3.65 (m, 4 H), 3.51 (dd, $J_{2,3}$ = 10.5, $J_{2,1}$ = 3.5 Hz, 1 H, 2-H), 3.48 (t, $J_{3,2}$ = $J_{3,4}$ = 9.5 Hz, 1 H, 4-H). $^{13}C$ NMR (62.9 MHz, DMSO, ppm): δ = 132.9 (C-b), 116.4 (C-c), 96.5 (C-1), 73.2, 70.9, 70.5, 67.1 (C-6), 63.0, 60.6 (C-2). $C_9H_{15}N_3O_5$ (245.2 g/mol): calcd. C 44.08, H 6.17, N 17.13; found C 44.57, H 6.32, N 16.52.

Benzaldehyde dimethyl acetal (13.7 mL, 91 mmol) and (±)-camphorsulfonic acid (1.42 g, 6.1 mmol) were added successively to a solution of crude compound **23** in acetonitrile (300 mL). The reaction mixture was stirred for 8 hours and quenched by addition of a satd. aqueous $NaHCO_3$ solution (100 mL). The resulting solution was then extracted with $Et_2O$ (3 × 200 mL), and the organic layers were combined, washed with water (3 × 150 mL), filtered through a silicon-treated filter, dried ($MgSO_4$), filtered, and concentrated. The residue was dissolved in the minimum of $Et_2O$, and crude **24** was precipitated by addition of petroleum ether. The solid recovered after filtration (17.7 g) was dissolved in $CH_2Cl_2$, filtered through a silica gel pad (petroleum ether/EtOAc/$CH_2Cl_2$, 75:15:10) and concentrated. Crystallisation ($Et_2O$/petroleum ether) gave a first crop of **24** (14.3 g) as white crystals. Flash chromatography of the combined mother liquors (petroleum ether/EtOAc/$CH_2Cl_2$, 90:5:5 to 75:15:10) and crystallisation gave another crop of **24** (2.3 g), thus corresponding to a combined yield of 50% from glucosamine hydrochloride **25**. m.p. 113 °C. $[\alpha]_D^{28} = -117$ ($c$ = 1.0, $CH_2Cl_2$). IR (KBr pellet, $cm^{-1}$): $\tilde{\nu}$ = 3400 (3520−3100, $\nu_{O-H}$), 3074, 3049, 3015, 2999, 2982 ($\nu_{C-H,arom}$), 2916, 2999, 2866 ($\nu_{C-H,aliph}$), 2104 ($\nu_{N3}$), 1452, 1427, 1373, 1327, 1309, 1269. $^1H$ NMR (250 MHz, $CDCl_3$, ppm): δ = 7.55−7.45 (m, 2 H, Ph), 7.45−7.35 (m, 3 H, Ph), 5.95 (dddd, $J_{b,ct}$ = 17.0, $J_{b,cc}$ = 10.5, $J_{b,a'}$ = 6.0, $J_{b,a}$ = 5.0 Hz, 1 H, H-b), 5.56 (s, 1 H, C*H*Ph), 5.37 (dq, $J_{ct,b}$ = 17.0, $J_{ct,a}$ = $J_{ct,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-ct), 5.27 (dq, $J_{cc,b}$ = 10.5, $J_{cc,a}$ = $J_{cc,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-cc), 4.98 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.32−4.20 (m, 3 H, 6-$H^a$, 3-H, H-a), 4.07 (ddt, $J_{gem}$ = 13.0, $J_{a',b}$ = 6.0, $J_{a',cc}$ = $J_{a',ct}$ = 1.5 Hz, 1 H, H-a′), 3.91 (td, $J_{5,4}$ = $J_{5,6b}$ = 9.5, $J_{5,6a}$ = 4.5 Hz, 1 H, H-5), 3.74 (t, $J_{6b,5}$ = $J_{6b,6a}$ = 9.5 Hz, 1 H, 6-$H^b$), 3.53 (t, $J_{4,3}$ = $J_{4,5}$ = 9.5 Hz, 1 H, 4-H), 3.31 (dd, $J_{2,3}$ = 10.0, $J_{2,1}$ = 3.5 Hz, 1 H, 2-H), 2.66 (d, $J_{OH,3}$ = 2.5 Hz, 1 H, OH). $^{13}C$ NMR (62.5 MHz, $CDCl_3$, ppm): δ = 136.8 ($C_{quaternary,arom}$), 133.0 (C-b), 129.3, 128.4, 126.2 ($C_{arom}$), 118.1 (C-c), 102.0 (*C*HPh), 97.5 (C-1), 81.8 (C-a), 68.8 (C-3, C-4, C-5), 63.0 (C-6), 62.4 (C-2). $C_{16}H_{19}N_3O_5$ (333.3 g/mol): calcd. C 57.65, H 5.75, N 12.61, O 24.00; found C 57.58, H 5.69, N 12.74, O 23.79.

**Allyl 2-Azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (28):** Compound **24** (16.21 g, 48.7 mmol) was dried azeotropically with toluene and dissolved in DMF (300 mL). NaH (60% in oil, 3.12 g, 78.1 mmol, 1.6 equiv.) and benzyl bromide (8.7 mL, 73.2 mmol, 1.5 equiv.) were successively added to this cooled solution (0 °C). After 35 min stirring at this temperature, the reaction mixture was quenched with *i*PrOH (10 mL), and water (10 mL) was added. The solution was diluted with diethyl ether (500 mL) and water (250 mL). The aqueous phase was further extracted with diethyl ether (2 × 250 mL), and the combined organic layers were washed with a 5% aqueous $KH_2PO_4$ solution (250 mL) and water (2 × 250 mL). The organic phase was dried ($MgSO_4$), filtered, and concentrated. Crystallisation from $Et_2O$/petroleum ether gave a first crop of white crystals (16.0 g), and the mother liquor was concentrated. Flash chromatography of the residue (petroleum ether/EtOAc, 95:5 to 8:2) followed by crystallisation gave an additional crop of **28** (4.3 g), giving a combined yield of 99%. m.p. 95 °C. $[\alpha]_D^{29} = -67$ ($c$ = 1.0, $CH_2Cl_2$). IR (KBr pellet, $cm^{-1}$): $\tilde{\nu}$ = 3096, 3070, 3037, 3012 ($\nu_{C-H,aliph}$), 2912, 2875 ($\nu_{C-H,aliph}$), 2107 ($\nu_{N3}$), 1497, 1453, 1371, 1308, 1233, 1214, 1175, 1127, 1088. $^1H$ NMR (250 MHz, $CDCl_3$, ppm): δ = 7.55−7.45 (m, 2 H, Ph), 7.45−7.25 (m, 8 H, Ph), 5.93 (dddd, $J_{b,ct}$ = 17.0, $J_{b,cc}$ = 10.5, $J_{b,a'}$ = 6.0, $J_{b,a}$ = 5.0 Hz, 1 H, H-b), 5.59 (s, 1 H, C*H*Ph), 5.35 (dq, $J_{ct,b}$ = 17.0, $J_{ct,a}$ = $J_{ct,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-ct), 5.25 (dq, $J_{cc,b}$ = 10.5, $J_{cc,a}$ = $J_{cc,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-cc), 4.96 (d, $J$ = 11.0 Hz, 1 H, C$H_2$Ph), 4.94 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.81 (d, $J$ = 11.0 Hz, 1 H, C$H_2$Ph), 4.28 (dd, $J_{6a,6b}$ = 10.0, $J_{6a,5}$ = 4.5 Hz, 1 H, 6-$H^a$), 4.22 (ddt, $J_{gem}$ = 13.0, $J_{a,b}$ = 5.0, $J_{a,cc}$ = $J_{a,ct}$ = 1.5 Hz, 1 H, H-a), 4.11 (t, $J_{6b,6a}$ = $J_{6b,5}$ = 10.0 Hz, 1 H, 6-$H^b$), 4.06 (ddt, $J_{gem}$ = 13.0, $J_{a',b}$ = 6.0, $J_{a',cc}$ = $J_{a',ct}$ = 1.5 Hz, 1 H, H-a′), 3.93 (td, $J_{5,6b}$ = $J_{5,4}$ = 10.0, $J_{5,6a}$ = 4.5 Hz, 1 H, 5-H), 3.76 (t, $J$ = 10.0 Hz, 1 H, 3-H or 4-H), 3.71 (t, $J$ = 10.0 Hz, 1 H, 3-H or 4-H), 3.41 (dd, $J_{2,3}$ = 10.0, $J_{2,1}$ = 3.5 Hz, 1 H, 2-H). $^{13}C$ NMR (62.5 MHz, $CDCl_3$, ppm): δ = 137.8, 137.2 (2 $C_{quaternary,arom}$), 133.1 (C-b), 129.1, 128.5, 128.3, 128.2, 127.9, 126.0 ($C_{arom}$), 118.2 (C-c), 101.4 (*C*H-Ph), 97.4 (C-1), 82.8 (C-a), 76.2, 75.0, 68.8, 68.7, 63.0 (C-6), 62.8 (C-2). $C_{23}H_{25}N_3O_5$ (423.5 g/mol): calcd. C 65.24, H 5.95, N 9.92, O 18.89; found C 64.95, H 5.96, N 9.98, O 18.63.

**Allyl 2-Azido-3-*O*-benzyl-2-deoxy-α-D-glucopyranoside (29):** Dowex 50X8 200 $H^+$ (7.0 g) was added to a solution of compound **28** (6.77 g, 16.0 mmol) in $CH_2Cl_2$ (45 mL) and MeOH (190 mL). After 24 h stirring at 40 °C, the mixture was filtered, neutralised with solid $NaHCO_3$ and again filtered, and the resulting solution was concentrated. Flash chromatography of the residue (petroleum ether/EtOAc, 8:2 to 1:1) gave compound **29** as an oil (5.27 g, quant). $[\alpha]_D^{29} = -112$ ($c$ = 1.1, $CH_2Cl_2$). IR (thin film, $cm^{-1}$): $\tilde{\nu}$ = 3411 (3600−3100, $\nu_{O-H}$), 3091, 3066, 3029 ($\nu_{C-H,aliph}$), 2924, 2874 ($\nu_{C-H,aliph}$), 2108 ($\nu_{N3}$), 1497, 1454, 1408, 1349, 1333, 1259, 1209 ($\nu_{C=C,arom}$). $^1H$ NMR (250 MHz, $CDCl_3$, ppm): δ = 7.35−7.30 (m, 5 H, Ph), 5.94 (dddd, $J_{b,ct}$ = 17.0, $J_{b,cc}$ = 10.5, $J_{b,a'}$ = 6.0, $J_{b,a}$ = 5.0 Hz, 1 H, H-b), 5.36 (dq, $J_{ct,b}$ = 17.0, $J_{ct,a}$ = $J_{ct,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-ct), 5.25 (dq, $J_{cc,b}$ = 10.5, $J_{cc,a}$ = $J_{cc,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-cc), 4.97 (d, $J$ = 11.5 Hz, 1 H, C$H_2$Ph), 4.96 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.74 (d, $J$ = 11.5 Hz, 1 H, C$H_2$Ph), 4.22 (ddt, $J_{gem}$ = 13.0, $J_{a,b}$ = 5.0, $J_{a,cc}$ = $J_{a,ct}$ = 1.5 Hz, 1 H, H-a), 4.05 (ddt, $J_{gem}$ = 13.0, $J_{a',b}$ = 6.0, $J_{a',cc}$ = $J_{a',ct}$ = 1.5 Hz, 1 H, H-a′), 3.92−3.75 (m, 3 H), 3.75−3.58 (m, 2 H), 3.31 (dd, $J_{2,3}$ = 10.0, $J_{2,1}$ = 3.5 Hz, 1 H, 2-H), 2.65 (br. s, 1 H, OH), 2.30 (br. s, 1 H, OH). $^{13}C$ NMR (62.5 MHz, $CDCl_3$, ppm): δ = 137.9 ($C_{quaternary,arom}$), 133.1 (C-b), 128.6, 128.1 ($C_{arom}$), 118.1 (C-c), 96.9 (C-1), 80.0 (C-a), 75.1 (*C*H$_2$Ph), 71.3, 70.7, 68.5, 62.9 (C-6), 61.9 (C-2). $C_{16}H_{21}N_3O_5$ (335.4 g/mol): calcd. C 57.38, H 6.31, N 12.53, O 23.85; found C 57.28, H 6.36, N 12.18, O 23.92.

**Allyl 6-*O*-Acetyl-2-azido-3-*O*-benzyl-2-deoxy-α-D-glucopyranoside (6):** Diol **29** (6.90 g, 20.6 mmol) was azeotropically dried with toluene (200 mL). AcCl (1.64 mL, 23 mmol, 1.1 equiv.) was then added dropwise to a cooled (0 °C) solution of this compound in pyridine (100 mL). After overnight stirring at 0 °C, the reaction mixture was quenched with MeOH (1 mL). The mixture was concentrated and the residue was dissolved in $Et_2O$ (500 mL). This solution was washed with aqueous $KH_2PO_4$ (2 M, 100 mL), water (2 × 100 mL), satd. aqueous $NaHCO_3$ (2 × 100 mL), and finally water (2 × 100 mL), dried ($MgSO_4$), filtered, and concentrated. Flash chromatography of the residue (petroleum ether/EtOAc, 9:1 to 7:3) yielded **6** (7.34 g, 95%) as a colourless oil. $[\alpha]_D^{29} = -121$ ($c$ = 2.8, $CH_2Cl_2$). IR (thin film, $cm^{-1}$): $\tilde{\nu}$ = 3431 (3600−3100, $\nu_{O-H}$), 3099, 3068, 3037 ($\nu_{C-H,arom}$), 2973, 2927, 2867 ($\nu_{C-H,aliph}$), 2109 ($\nu_{N3}$), 1735, 1658, 1455, 1376, 1257, 1146, 1091. $^1$H NMR (250 MHz, $CDCl_3$, ppm): δ = 7.45−7.30 (m, 5 H, Ph), 5.94 (dddd, $J_{b,ct}$ = 17.0, $J_{b,cc}$ = 10.5, $J_{b,a'}$ = 6.5, $J_{b,a}$ = 5.5 Hz, 1 H, H-b), 5.35 (dq, $J_{ct,b}$ = 17.0, $J_{ct,a} = J_{ct,a'} = J_{gem}$ = 1.5 Hz, 1 H, H-ct), 5.25 (dq, $J_{cc,b}$ = 10.5, $J_{cc,a} = J_{cc,a'} = J_{gem}$ = 1.5 Hz, 1 H, H-cc), 4.96 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.93 (d, $J$ = 11.0 Hz, 1 H, C$H_2$Ph), 4.82 (d, $J$ = 11.0 Hz, 1 H, C$H_2$Ph), 4.54 (dd, $J_{6a,6b}$ = 12.5, $J_{6a,5}$ = 4.0 Hz, 1 H, 6-H$^a$), 4.21 (ddt, $J_{gem}$ = 13.0, $J_{a,b}$ = 5.5, $J_{a,cc} = J_{a,ct}$ = 1.5 Hz, 1 H, H-a), 4.17 (dd, $J_{6b,6a}$ = 12.5, $J_{6b,5}$ = 2.5 Hz, 1 H, 6-H$^b$), 4.06 (ddt, $J_{gem}$ = 13.0, $J_{a',b}$ = 6.5, $J_{a',cc} = J_{a',ct}$ = 1.5 Hz, 1 H, H-a′), 3.87 (dd, $J_{3,2}$ = 10.0, $J_{3,4}$ = 8.5 Hz, 1 H, 3-H), 3.81 (ddd, $J_{5,4}$ = 10.0, $J_{5,6a}$ = 4.0, $J_{5,6b}$ = 2.5 Hz, 1 H, 5-H), 3.48 (ddd, $J_{4,5}$ = 10.0, $J_{4,3}$ = 8.5, $J_{4,OH}$ = 3.5 Hz, 1 H, 4-H), 3.34 (dd, $J_{2,3}$ = 10.0, $J_{2,1}$ = 3.5 Hz, 1 H, 2-H), 2.73 (d, $J_{OH,4}$ = 3.5 Hz, 1 H, OH), 2.12 (s, 3 H, C$H_3$ OAc). $^{13}$C NMR (62.5 MHz, $CDCl_3$, ppm): δ = 171.7 (C=O), 137.8 ($C_{quaternary,arom}$), 133.0 (C-b), 128.6, 128.2, 128.1 ($C_{arom}$), 118.2 (C-c), 96.8 (C-1), 79.5 (C-a), 75.2 (*C*H$_2$Ph), 70.5, 70.0, 68.6, 62.8 (C-6, C-2), 20.8 (*C*H$_3$, OAc). $C_{18}H_{23}N_3O_6$ (377.4 g/mol): calcd. C 57.29, H 6.14, N 11.13; found C 56.96, H 6.15, N 10.71.

**Allyl 2-Azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (7):** $NaBH_3CN$ (1.196 g, 19.03 mmol, 8 equiv.) was added to a cooled (0 °C) suspension of compound **28** (4.67 g, 11.3 mmol), molecular sieves (4 Å, 12 g) and a spatula tip of methyl orange in THF (40 m L). A satd. ethereal HCl solution (≈ 75 mL) was then added to the reaction mixture until the solution became a persistent pink. After 10 minutes at 0 °C, the reaction was quenched with a satd. aqueous $NaHCO_3$ solution (100 mL) and diluted with diethyl ether (250 mL). The aqueous phase was extracted with $Et_2O$ (100 mL) and the combined organic layers were washed twice with water (100 mL), dried ($MgSO_4$), filtered, and concentrated. Flash chromatography of the residue (petroleum ether/EtOAc, 8:2 to 6:4) gave compound **7** (4.33 g, 90%) as a colourless oil. $[\alpha]_D^{29}$ = 79 ($c$ = 1.1, $CH_2Cl_2$). IR (thin film, $cm^{-1}$): $\tilde{\nu}$ = 3457 (3600−3200, $\nu_{O-H}$), 3086, 3062, 3032 ($\nu_{C-H,arom}$), 2916, 2868 ($\nu_{C-H,aliph}$), 2111 ($\nu_{N3}$), 1496, 1453, 1363, 1332, 1262, 1051. $^1$H NMR (250 MHz, $CDCl_3$, ppm): δ = 7.50−7.28 (m, 10 H, Ph), 5.94 (dddd, $J_{b,ct}$ = 17.0, $J_{b,cc}$ = 10.5, $J_{b,a'}$ = 6.5, $J_{b,a}$ = 5.0 Hz, 1 H, H-b), 5.34 (dq, $J_{ct,b}$ = 17.0, $J_{ct,a} = J_{ct,a'} = J_{gem}$ = 1.5 Hz, 1 H, H-ct), 5.24 (dq, $J_{cc,b}$ = 10.5, $J_{cc,a} = J_{cc,a'} = J_{gem}$ = 1.5 Hz, 1 H, H-cc), 4.95 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.93 (d, $J$ = 11.0 Hz, 1 H, C$H_2$Ph), 4.80 (d, $J$ = 11.0 Hz, 1 H, C$H_2$Ph), 4.62 (d, $J$ = 12.0 Hz, 1 H, C$H_2$Ph), 4.54 (d, $J$ = 12.0 Hz, 1 H, C$H_2$Ph), 4.22 (ddt, $J_{gem}$ = 13.0, $J_{a,b}$ = 5.0, $J_{a,cc} = J_{a,ct}$ = 1.5 Hz, 1 H, H-a), 4.05 (ddt, $J_{gem}$ = 13.0, $J_{a',b}$ = 6.5, $J_{a',cc} = J_{a',ct}$ = 1.5 Hz, 1 H, H-a′), 3.92−3.66 (m, 4 H, 3-H, 4-H, 5-H, 6-H$^a$), 3.66 (dd, $J_{6b,6a}$ = 10.0, $J_{6b,5}$ = 4.0 Hz, 1 H, 6-H$^b$), 3.36 (dd, $J_{2,3}$ = 10.0, $J_{2,1}$ = 3.5 Hz, 1 H, 2-H), 2.48 (d, $J_{OH,4}$ = 2.5 Hz, 1 H, OH). $^{13}$C NMR (62.5 MHz, $CDCl_3$, ppm): δ = 137.9, 137.5 (2 $C_{quaternary,arom}$), 133.1 (C-b), 128.5, 128.2, 127.6, 127.5, 127.1 ($C_{arom}$), 117.6 (C-c), 96.6 (C-1), 79.6 (C-3), 74.6 (*C*H$_2$Ph), 73.3 (*C*H$_2$Ph), 71.6 (C-4), 70.2 (C-5), 69.3 (C-a), 68.1 (C-6), 62.5 (C-2). $C_{23}H_{27}N_3O_5$ (425.5 g/mol): calcd. C 64.93, H 6.49, N 9.88, O 18.90; found C 64.74, H 6.41, N 9.97, O 18.93.

**Allyl [Methyl 2-*O*-acetyl-3-*O*-benzyl-4-*O*-(4-methoxybenzyl)-α-L-idopyranosyluronate]-(1→4)-*O*-6-*O*-acetyl-2-azido-3-*O*-benzyl-2-deoxy-α-D-glucopyranoside (1). From 4 and 6:** Imidate **4** (3.78 g, 6.2 mmol) and acceptor **6** (4.7 g, 12.5 mmol, 2 equiv.) were azeotropically dried with toluene and dissolved in $CH_2Cl_2$ (15 mL). Powdered molecular sieve (4 Å, 13.5 g) was added and the mixture was then stirred for 30 min at room temp. TMSOTf (0.1 M in $CH_2Cl_2$, 9.4 mL, 0.94 mmol, 0.15 equiv.) was added and, after 5 min stirring, the reaction mixture was quenched with satd. aqueous $NaHCO_3$ solution (20 mL), diluted with water (100 mL), and extracted with EtOAc (3 × 200 mL). The combined organic layers were concentrated and the residue was purified by flash chromatography (petroleum ether/$CH_2Cl_2$/EtOAc, 5:90:5 to 5:15:80), giving compound **1** as a colourless oil (3.0 g, 60%), together with recovered compound **6** (2 g). $[\alpha]_D^{28}$ = 20 ($c$ = 1.0, $CH_2Cl_2$). IR (thin film, $cm^{-1}$): $\tilde{\nu}$ = 3063, 3032 ($\nu_{C-H,arom}$), 2950, 2935 ($\nu_{C-H,aliph}$), 2109 ($\nu_{N3}$), 1740 ($\nu_{C=O}$), 1613, 1514, 1455, 1439, 1373, 1303, 1244. $^1$H NMR (400 MHz, $CDCl_3$, ppm): δ = 7.52−7.36 (m, 10 H, Ph), 7.25 (d, $J$ = 8.5 Hz, 2 H, *Ph*-OMe), 6.96 (d, $J$ = 8.5 Hz, 2 H, *Ph*-OMe), 6.06 (dddd, $J_{b,ct}$ = 17.0, $J_{b,cc}$ = 11.0, $J_{b,a'}$ = 6.0, $J_{b,a}$ = 5.0 Hz, 1 H, H-b), 5.49 (dq, $J_{ct,b}$ = 17.0, $J_{ct,a} = J_{ct,a'} = J_{gem}$ = 1.5 Hz, 1 H, H-ct), 5.39 (dq, $J_{cc,b}$ = 11.0, $J_{cc,a} = J_{cc,a'} = J_{gem}$ = 1.5 Hz, 1 H, H-cc), 5.38 (d, $J_{1',2'}$ = 5.0 Hz, 1 H, 1′-H), 5.05 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 5.02 (t, $J_{2',3'} = J_{2',1'}$ = 5.0 Hz, 1 H, 2′-H), 5.02 (d, $J$ = 10.5 Hz, 1 H, C$H_2$Ph), 4.83 (d, $J$ = 11.0 Hz, 1 H, C$H_2$Ph), 4.82 (d, $J$ = 10.5 Hz, 1 H, C$H_2$Ph), 4.81 (d, $J_{5',4'}$ = 6.5 Hz, 1 H, 5′-H), 4.78 (d, $J$ = 11.0 Hz, 1 H, C$H_2$Ph), 4.58 (d, $J$ = 11.5 Hz, 1 H, C$H_2$PhOMe), 4.52 (d, $J$ = 11.5 Hz, 1 H, C$H_2$PhOMe), 4.50 (dd, $J_{6a,6b}$ = 12.5, $J_{6a,5}$ = 2.0 Hz, 1 H, 6-H$^a$), 4.36 (dd, $J_{6b,6a}$ = 12.5, $J_{6b,5}$ = 3.5 Hz, 1 H, 6-H$^b$), 4.37 (ddt, $J_{gem}$ = 13.0, $J_{a,b}$ = 5.0, $J_{a,cc} = J_{a,ct}$ = 1.5 Hz, 1 H, H-a), 4.17 (ddt, $J_{gem}$ = 13.0, $J_{a',b}$ = 6.0, $J_{a',cc} = J_{a',ct}$ = 1.5 Hz, 1 H, H-a′), 4.10 (dd, $J_{4,5}$ = 9.5, $J_{4,3}$ = 9.0, 1 H, 4-H), 4.02 (dd, $J_{3,2}$ = 10.0, $J_{3,4}$ = 9.0 Hz, 1 H, 3-H), 3.98 (ddd, $J_{5,4}$ = 9.5, $J_{5,6b}$ = 3.5, $J_{5,6a}$ = 2.0 Hz, 1 H, 5-H), 3.95−3.90 (m, 4 H, containing s at δ = 3.92, 4′-H and OMe), 3.88 (t, $J_{3',2'} = J_{3',4'}$ = 5.0, 1 H, 3′-H), 3.66 (s, 3 H, OMe), 3.54 (dd, $J_{2,3}$ = 10.0, $J_{2,1}$ = 3.5 Hz, 1 H, 2-H), 2.20 (s, 3 H, C$H_3$ OAc), 2.18 (s, 3 H, C$H_3$ OAc). $^{13}$C NMR (62.5 MHz, $CDCl_3$, ppm): δ = 170.7, 170.0, 169.8 (C=O), 159.3 (*C*-OMe, *p*MBn), 137.9, 137.7 ($C_{quaternary,arom}$), 133.0 (C-b), 129.5, 129.3, 128.4, 128.1, 127.9, 127.8, 127.4 ($C_{arom}$), 118.2 (C-c), 113.7 ($C_m$ *p*MBn), 97.9 (C′-1), 96.5 (C-1), 78.2 (C-3), 75.7 (C-4), 74.9 (*C*H$_2$Ph), 74.7 (C′-3), 74.4 (C′-4), 73.0 (*C*H$_2$Ph), 72.4 (*C*H$_2$ *p*MBn), 70.5 (C′-5), 70.1 (C′-2), 69.1 (C-5), 68.6 (C-a), 63.1 (C-2), 62.0 (C-2), 55.2 (*C*H$_3$ OMe *p*MBn), 51.7 (*C*H$_3$, COOMe), 20.9, 20.7 (*C*H$_3$, OAc). $C_{42}H_{49}N_3O_{14}$ (819.9 g/mol): calcd. C 61.53, H 6.02, N 5.13, O 27.32; found C 61.22, H 5.96, N 4.97, O 27.04.

**Allyl (Methyl 2,4-di-*O*-acetyl-3-*O*-benzyl-α-L-idopyranosyluronate)-(1→4)-*O*-6-*O*-acetyl-2-azido-3-*O*-benzyl-2-deoxy-α-D-glucopyranoside (30):** Bromide donor **5** (1.0 g, 2.2 mmol) and acceptor **6** (1.2 g, 3.1 mmol, 1.4 equiv.) were azeotropically dried with toluene. Compound **4** was dissolved in $CH_2Cl_2$ (20 mL) and transferred to a reaction flask containing **6** and powdered molecular sieves (4 Å, 900 mg). The resulting mixture was stirred for 30 min at room temp. and then cooled to 0 °C, and AgOTf (203 mg, 792 mmol, 1.2 equiv.) was added. After 1.5 h stirring at this temperature, the reaction mixture was diluted with $CH_2Cl_2$ (50 mL), filtered through a Celite 545 pad and concentrated. Flash chromatography of the residue (petroleum ether/EtOAc, 7:3 to 3:7) gave disaccharide **30** (1.1 g,

65%), together with recovered acceptor **6** (520 mg). $[\alpha]_D^{29}$ = 19 (*c* = 5.8, $CH_2Cl_2$). IR (thin film, $cm^{-1}$): $\tilde{\nu}$ = 3064, 3033 ($\nu_{C-H,arom}$), 2952, 2929, 2874 ($\nu_{C-H,aliph}$), 2110 ($\nu_{N3}$), 1747 ($\nu_{C=O}$), 1455, 1438, 1373, 1228. $^1$H NMR (250 MHz, $CDCl_3$, ppm): δ = 7.45−7.10 (m, 10 H, Ph), 5.95 (dddd, $J_{b,ct}$ = 17.0, $J_{b,cc}$ = 10.0, $J_{b,a'}$ = 6.0, $J_{b,a}$ = 5.0 Hz, 1 H, H-b), 5.37 (dq, $J_{ct,b}$ = 17.0, $J_{ct,a}$ = $J_{ct,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-ct), 5.28 (dq, $J_{cc,b}$ = 10.0, $J_{cc,a}$ = $J_{cc,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-cc), 5.14 (d, $J_{1',2'}$ = 2.0 Hz, 1 H, 1′-H), 5.06 (dd, $J_{4',5'}$ = 3.0, $J_{4',3'}$ = 2.5 Hz, 1 H, 4′-H), 4.96 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.92 (d, $J_{5',4'}$ = 3.0 Hz, 1 H, 5′-H), 4.88 (dd, $J_{2',3'}$ = 2.5, $J_{2',1'}$ = 2.0 Hz, 1 H, 2′-H), 4.75 (d, *J* = 12.0 Hz, 1 H, C*H*$_2$Ph), 4.70 (d, *J* = 12.0 Hz, 1 H, C*H*$_2$Ph), 4.70 (d, *J* = 10.0 Hz, 1 H, C*H*$_2$Ph), 4.65 (d, *J* = 10.0 Hz, 1 H, C*H*$_2$Ph), 4.45 (dd, $J_{6a,6b}$ = 12.0, $J_{6a,5}$ = 1.5 Hz, 1 H, 6-H[a]), 4.28−4.16 (m, 2 H, 6-H[b] and H-a), 4.06 (ddt, $J_{gem}$ = 13.0, $J_{a',b}$ = 6.0, $J_{a',cc}$ = $J_{a',ct}$ = 1.5 Hz, 1 H, H-a′), 3.95−3.75 (m, 4 H, 3-H, 4-H, 5-H and 3′-H), 3.43 (dd, $J_{2,3}$ = 10.0, $J_{2,1}$ = 3.5 Hz, 1 H, 2-H), 3.42 (s, 3 H, OMe), 2.11 (s, 3 H, C*H*$_3$ OAc), 2.02 (s, 3 H, C*H*$_3$ OAc), 1.95 (s, 3 H, C*H*$_3$ OAc). $^{13}$C NMR (62.5 MHz, $CDCl_3$, ppm): δ = 170.6, 169.9, 169.8, 168.7 (C=O), 137.7, 137.2 ($C_{quaternary,arom}$), 133.1 (C-b), 128.5, 128.0, 127.5, 127.4 ($C_{arom}$), 118.4 (C-c), 97.5 (C′-1), 96.5 (C-1), 78.4, 74.8, 74.7 (*C*H$_2$Ph), 72.6 (*C*H$_2$Ph), 72.8, 69.3, 68.7 (C-a), 68.0, 67.6, 67.0, 63.4 (C-2), 62.0 (C-6), 52.2 (*C*H$_3$, COOMe), 20.9, 20.8, 20.7 (*C*H$_3$, OAc). $C_{36}H_{43}N_3O_{14}$ (741.7 g/mol): calcd. C 58.29, H 5.84, N 5.66, O 30.20; found C 58.01, H 5.81, N 5.44, O 30.12.

**Allyl (Methyl 2,4-di-*O*-acetyl-3-*O*-benzyl-α-L-idopyranosyluronate)-(1→4)-*O*-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (31):** Acceptor **7** (300 mg; 0.67 mmol) and donor **5** (400 mg, 0.94 mmol, 1.4 equiv.) were treated as described above, giving disaccharide **31** (425 mg, 81%), together with recovered acceptor **7** (170 mg). $[\alpha]_D^{27}$ = 12 (*c* = 3.3, $CH_2Cl_2$). IR (thin film, $cm^{-1}$): $\tilde{\nu}$ = 3077, 3061, 3030 ($\nu_{C-H,arom}$), 2952, 2921, 2874, 2858 ($\nu_{C-H,aliph}$), 2102 ($\nu_{N3}$), 1736 ($\nu_{C=O}$), 1497, 1455, 1439, 1373, 1226, 1253, 1222. $^1$H NMR (200 MHz, $CDCl_3$, ppm): δ = 7.45−7.15 (m, 10 H, Ph), 5.95 (dddd, $J_{b,ct}$ = 17.0, $J_{b,cc}$ = 10.5, $J_{b,a'}$ = 6.0, $J_{b,a}$ = 5.0 Hz, 1 H, H-b), 5.35 (dq, $J_{ct,b}$ = 17.0, $J_{ct,a}$ = $J_{ct,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-ct), 5.25 (dq, $J_{cc,b}$ = 10.5, $J_{cc,a}$ = $J_{cc,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-cc), 5.20 (br. s, 1 H, 1′-H), 5.04 (dd, $J_{4',3'}$ = 3.0, $J_{4',5'}$ = 2.5 Hz, 1 H, 4′-H), 4.97 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.94 (d, $J_{5',4'}$ = 2.5 Hz, 1 H, 5′-H), 4.92−4.87 (m, 1 H, 2′-H), 4.73 (s, 2 H, C*H*$_2$Ph), 4.63 (s, 2 H, C*H*$_2$Ph), 4.61 (d, *J* = 12.0 Hz, 1 H, C*H*$_2$Ph), 4.51 (d, *J* = 12.0 Hz, 1 H, C*H*$_2$Ph), 4.21 (ddt, $J_{gem}$ = 13.0, $J_{a,b}$ = 5.0, $J_{a,cc}$ = $J_{a,ct}$ = 1.5 Hz, 1 H, H-a), 4.04 (ddt, $J_{gem}$ = 13.0, $J_{a',b}$ = 6.0, $J_{a',cc}$ = $J_{a',ct}$ = 1.5 Hz, 1 H, H-a′), 4.04 (dd, $J_{6a,6b}$ = 9.0, $J_{6a,5}$ = 1.0 Hz, 1 H, 6-H[a]), 3.89−3.74 (m, 4 H, 3-H, 4-H, 5-H and 3′-H), 3.65 (dd, $J_{6b,6a}$ = 9.0, $J_{6b,5}$ = 3.0 Hz, 1 H, 6-H[b]), 3.45 (dd, $J_{2,3}$ = 10.0, $J_{2,1}$ = 3.5 Hz, 1 H, 2-H), 3.35 (s, 3 H, OMe), 2.00 (s, 3 H, C*H*$_3$ OAc), 1.99 (s, 3 H, C*H*$_3$ OAc). $^{13}$C NMR (62.5 MHz, $CDCl_3$, ppm): δ = 169.9, 169.7, 168.4 (C=O), 137.9, 137.8, 137.2 ($C_{quaternary,arom}$), 133.2 (C-b), 128.4, 128.3, 128.1, 127.6, 127.5, 127.1 ($C_{arom}$), 118.0 (C-c), 97.1 (C′-1), 96.6 (C-1), 78.4, 74.4, 74.2, 73.1, 72.5, 72.2, 70.9, 68.5, 67.9, 67.1, 63.3, 63.5, 51.9 (*C*H$_3$, COOMe), 20.8, 20.7 (*C*H$_3$, OAc). $C_{41}H_{47}N_3O_{13}$ (789.8 g/mol): calcd. C 62.35, H 6.00, N 5.32, O 26.33; found C 62.31, H 5.82, N 4.97, O 26.45.

**Allyl (Methyl 3-*O*-benzyl-α-L-idopyranosyluronate)-(1→4)-*O*-2-azido-3-*O*-benzyl-2-deoxy-α-D-glucopyranoside (32):** Dried $K_2CO_3$ (16 mg, 0.11 mmol, 0.3 equiv.) was added to a solution of disaccharide **30** (296 mg, 0.39 mmol) in MeOH (5 mL). The reaction mixture was stirred at room temp. for one night, filtered, neutralised with Dowex 50X8 200 $H^+$ and again filtered, and the methanol was evaporated. Flash chromatography of the residue (petroleum ether/EtOAc/MeOH, 1:9:0.5) gave the disaccharide **32** (210 mg, 87%). $[\alpha]_D^{30}$ = 47 (*c* = 1.3, $CH_2Cl_2$). IR (thin film, $cm^{-1}$): $\tilde{\nu}$ = 3460 (3600−3100, $\nu_{O-H}$), 3087, 3065, 3032 ($\nu_{C-H,arom}$), 2949, 2926, 2856 ($\nu_{C-H,aliph}$), 2108 ($\nu_{N3}$), 1741 ($\nu_{C=O}$), 1497, 1455, 1366, 1263, 1216, 1154, 1105, 1043. $^1$H NMR (250 MHz, $CDCl_3$, ppm): δ = 7.45−7.10 (m, 10 H, Ph), 5.96 (dddd, $J_{b,ct}$ = 17.0, $J_{b,cc}$ = 10.0, $J_{b,a'}$ = 6.0, $J_{b,a}$ = 5.0 Hz, 1 H, H-b), 5.37 (dq, $J_{ct,b}$ = 17.0, $J_{ct,a}$ = $J_{ct,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-ct), 5.26 (dq, $J_{cc,b}$ = 10.0, $J_{cc,a}$ = $J_{cc,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-cc), 5.17 (br. s, 1 H, 1′-H), 4.96 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.78 (br. s, 1 H, 5′-H), 4.70 (d, *J* = 11.5 Hz, 1 H, C*H*$_2$Ph), 4.63 (d, *J* = 11.0 Hz, 1 H, C*H*$_2$Ph), 4.60 (d, *J* = 11.5 Hz, 1 H, C*H*$_2$Ph), 4.56 (d, *J* = 11.0 Hz, 1 H, C*H*$_2$Ph), 4.21 (ddt, $J_{gem}$ = 13.0, $J_{a,b}$ = 5.0, $J_{a,cc}$ = $J_{a,ct}$ = 1.5 Hz, 1 H, H-a), 4.04 (ddt, $J_{gem}$ = 13.0, $J_{a',b}$ = 6.0, $J_{a',cc}$ = $J_{a',ct}$ = 1.5 Hz, 1 H, H-a′), 4.03−3.91 (m, 4 H), 4.87−3.70 (m, 4 H), 3.40 (dd, $J_{2,3}$ = 10.0, $J_{2,1}$ = 3.5 Hz, 1 H, 2-H), 3.38 (s, 3 H, OMe). $^{13}$C NMR (62.5 MHz, $CDCl_3$, ppm): δ = 170.8 (C=O), 137.9, 137.6 ($C_{quaternary,arom}$), 133.2 (C-b), 128.4, 128.1, 128.0, 127.3, 127.1 ($C_{arom}$), 118.0 (C-c), 99.9 (C′-1), 96.7 (C-1), 78.5, 74.9, 74.4 (*C*H$_2$Ph), 73.9, 72.1 (*C*H$_2$Ph), 71.6, 68.6, 68.5 (C-a), 66.1, 63.6 (C-2), 60.7 (C-6), 52.0 (*C*H$_3$, COOMe). $C_{30}H_{37}N_3O_{11}$ (657.7 g/mol): calcd. C 58.53, H 6.06, N 6.83, O 28.59; found C 57.94, H 6.25, N 6.07, O 28.51. ESI MS calcd. for $C_{30}H_{37}N_3NaO_{11}$ [M + Na]: 638.2; found 638.2.

**Allyl (Methyl 3-*O*-benzyl-α-L-idopyranosyluronate)-(1→4)-*O*-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (33):** Disaccharide **31** (335 mg, 0.450 mmol) was treated as in the case of compound **30**. Flash chromatography (petroleum ether/EtOAc/MeOH, 1:9:0.5) gave disaccharide **33** (280 mg, 90%). IR (thin film, $cm^{-1}$): $\tilde{\nu}$ = 3448 (3600−3100, $\nu_{O-H}$), 3085, 3064, 3031 ($\nu_{C-H,arom}$), 2955, 2924, 2854 ($\nu_{C-H,aliph}$), 2107 ($\nu_{N3}$), 1740 ($\nu_{C=O}$), 1497, 1457, 1376, 1220, 1162. $^1$H NMR (250 MHz, $CDCl_3$, ppm): δ = 7.40−7.20 (m, 15 H, Ph), 5.95 (dddd, $J_{b,ct}$ = 17.0, $J_{b,cc}$ = 10.0, $J_{b,a'}$ = 6.0, $J_{b,a}$ = 5.0 Hz, 1 H, H-b), 5.36 (dq, $J_{ct,b}$ = 17.0, $J_{ct,a}$ = $J_{ct,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-ct), 5.25 (dq, $J_{cc,b}$ = 10.0, $J_{cc,a}$ = $J_{cc,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-cc), 5.06 (br. d, $J_{1',2'}$ = 2.0 Hz, 1 H, 1′-H), 4.97 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.73 (d, $J_{5',4'}$ = 2.5 Hz, 1 H, 5′-H), 4.72 (d, *J* = 10.5 Hz, 1 H, C*H*$_2$Ph), 4.67 (d, *J* = 11.0 Hz, 1 H, C*H*$_2$Ph), 4.64 (d, *J* = 10.5 Hz, 1 H, C*H*$_2$Ph), 4.62 (d, *J* = 11.0 Hz, 1 H, C*H*$_2$Ph), 4.60 (d, *J* = 12.0 Hz, 1 H, C*H*$_2$Ph), 4.53 (d, *J* = 12.0 Hz, 1 H, C*H*$_2$Ph), 4.21 (ddt, $J_{gem}$ = 13.0, $J_{a,b}$ = 5.0, $J_{a,cc}$ = $J_{a,ct}$ = 1.5 Hz, 1 H, H-a), 4.05 (ddt, $J_{gem}$ = 13.0, $J_{a',b}$ = 6.0, $J_{a',cc}$ = $J_{a',ct}$ = 1.5 Hz, 1 H, H-a′), 4.00 (t, $J_{4,3}$ = $J_{4,5}$ = 9.5 Hz, 1 H, 4-H), 4.00−3.92 (m, 1 H), 3.90−3.78 (m, 2 H), 3.72 (dd, $J_{6a,6b}$ = 11.0, $J_{6a,5}$ = 3.0 Hz, 1 H, 6-H[a]), 3.72−3.63 (m, 2 H), 3.63 (dd, $J_{6b,6a}$ = 11.0, $J_{6b,5}$ = 2.5 Hz, 1 H, 6-H[b]), 3.43 (dd, $J_{2,3}$ = 10.0, $J_{2,1}$ = 3.5 Hz, 1 H, 2-H), 3.42 (s, 3 H, OMe). $^{13}$C NMR (62.5 MHz, $CDCl_3$, ppm): δ = 170.5 (C=O), 138.0, 137.7, 137.6 ($C_{quaternary,arom}$), 133.3 (C-b), 128.5, 128.4, 128.1, 128.0, 127.8, 127.4, 127.2 ($C_{arom}$), 118.0 (C-c), 100.7 (C′-1), 96.7 (C-1), 78.5, 76.1, 75.5, 74.3 (*C*H$_2$Ph), 73.6 (*C*H$_2$Ph), 72.5 (*C*H$_2$Ph), 70.8, 68.9, 68.7, 68.5/68.4 (C-a/C-6), 67.8, 63.4 (C-2), 52.0 (*C*H$_3$, COOMe). ESI HR-MS calcd. for $C_{37}H_{43}N_3NaO_{11}$ [M + Na]: 728.27953; found 728.27941.

**Allyl (Methyl 2-*O*-acetyl-3-*O*-benzyl-α-L-idopyranosyluronate)-(1→4)-*O*-6-*O*-acetyl-2-azido-3-*O*-benzyl-2-deoxy-α-D-glucopyranoside (34):** A suspension of **32** (400 mg, 0.66 mmol) and $Bu_2SnO$ (360 mg, 1.45 mmol, 2.2 equiv.) in benzene (9 mL) was heated at 90 °C for 30 min. The temperature was then raised, and benzene (7 mL) was distilled off over 30 min (Dean−Stark apparatus). Acetyl chloride (117 μL, 1.65 mmol, 2.5 equiv.) and enough triethylamine to reach pH 8 (roughly 400 μL, 2.9 mmol, 4.4 equiv.) were then added and the reaction mixture was stirred at room temp. for 1 h. TLC (petroleum ether/EtOAc, 2:8, $R_{f32}$ = 0.09) showed the formation of the expected diacetate **34** ($R_f$ = 0.39), its 4′-*O*-acetyl-

ated regioisomer ($R_f$ = 0.54) and a triacetylated compound ($R_f$ = 0.60). The reaction mixture was directly placed on the top of a flash chromatography column and eluted (petroleum ether/EtOAc, 8:2 to 6:4), giving **34** (277 mg, 60%). The regioisomer of **34** and the triacetylated derivative were deacetylated as described for compound **30** and reacetylated as described above, giving another crop of **34** (69 mg), giving an overall yield of 75%. $[\alpha]_D^{27}$ = 37 (*c* = 1.0, $CH_2Cl_2$). IR (thin film, $cm^{-1}$): $\tilde{\nu}$ = 3490 (3650−3250, $\nu_{O-H}$), 3086, 3064, 3031 ($\nu_{C-H,arom}$), 2956, 2919, 2867 ($\nu_{C-H,aliph}$), 2106 ($\nu_{N3}$), 1744 ($\nu_{C=O}$), 1497, 1455, 1438, 1371, 1237, 1156, 1105, 1068, 1039. $^1$H NMR (250 MHz, $CDCl_3$, ppm): δ = 7.42−7.22 (m, 10 H, Ph), 5.96 (dddd, $J_{b,ct}$ = 17.0, $J_{b,cc}$ = 10.0, $J_{b,a'}$ = 6.0, $J_{b,a}$ = 5.5 Hz, 1 H, H-b), 5.37 (dq, $J_{ct,b}$ = 17.0, $J_{ct,a}$ = $J_{ct,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-ct), 5.28 (dq, $J_{cc,b}$ = 10.0, $J_{cc,a}$ = $J_{cc,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-cc), 5.07 (br. s, 1 H, 1′-H), 4.96 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.94 (dt, $J_{2'-3'}$ = 2.5, $J_{2',1'}$ = $J_{2',4'}$ = 1.0 Hz, 1 H, 2′-H), 4.90 (d, $J_{5',4'}$ = 2.5 Hz, 1 H, 5′-H), 4.75 (d, *J* = 11.5 Hz, 1 H, C$H_2$Ph), 4.75 (d, *J* = 10.5 Hz, 1 H, C$H_2$Ph), 4.66 (d, *J* = 10.5 Hz, 1 H, C$H_2$Ph), 4.63 (d, *J* = 11.5 Hz, 1 H, C$H_2$Ph), 4.42 (dd, $J_{6a,6b}$ = 11.5, $J_{6a,5}$ = 1.5 Hz, 1 H, 6-H$^a$), 4.23 (dd, $J_{6b,6a}$ = 11.5, $J_{6b,5}$ = 1.0 Hz, 1 H, 6-H$^b$), 4.22 (ddt, $J_{gem}$ = 13.0, $J_{a,b}$ = 5.5, $J_{a,cc}$ = $J_{a,ct}$ = 1.5 Hz, 1 H, H-a), 4.06 (ddt, $J_{gem}$ = 13.0, $J_{a',b}$ = 6.0, $J_{a',cc}$ = $J_{a',ct}$ = 1.5 Hz, 1 H, H-a′), 3.96 (br. d, $J_{4',OH}$ = 11.5 Hz, 1 H, 4′-H), 3.91−3.79 (m, 3 H, 3-H, 4-H, 5-H), 3.72 (ddd, $J_{3',4'}$ = 3.5, $J_{3',2'}$ = 2.5, $J_{3',1'}$ = 1.0 Hz, 1 H, 3′-H), 3.46 (s, 3 H, OMe), 3.40 (dd, $J_{2,3}$ = 10.0, $J_{2,1}$ = 3.5 Hz, 1 H, 2-H), 2.65 (d, $J_{OH,4'}$ = 11.5 Hz, 1 H, OH), 2.10 (s, 3 H, C$H_3$ OAc), 2.08 (s, 3 H, C$H_3$ OAc). $^{13}$C NMR (62.5 MHz, $CDCl_3$, ppm): δ = 170.5, 169.4, 169.1 (C=O), 137.7, 137.1 ($C_{quaternary,arom}$), 133.0 (C-b), 128.4, 128.1, 128.0, 127.4, 127.3 ($C_{arom}$), 118.3 (C-c), 97.9 (C′-1), 96.5 (C-1), 78.4, 75.0, 74.4 (*C*$H_2$Ph), 74.3, 72.3 (*C*$H_2$Ph), 69.1, 68.7 (C-a), 68.5, 67.6, 67.0, 63.5 (C-2), 62.1 (C-6), 52.0 (*C*$H_3$, COOMe), 20.8 (*C*$H_3$, OAc). $C_{34}H_{41}N_3O_{13}$ (699.7 g/mol): calcd. C 58.36, H 5.91, N 6.01, O 29.73; found C 58.39, H 5.93, N 5.66, O 30.11.

**Allyl (Methyl 2-*O*-acetyl-3-*O*-benzyl-α-L-idopyranosyluronate)-(1→4)-*O*-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (35):** Compound **33** (200 mg, 0.284 mmol) was treated as described for **32**, with $Bu_2SnO$ (85 mg, 0.340 mmol, 1.2 equiv.) and then acetyl chloride (24 μL, 0.340 mmol, 1.2 equiv.), without addition of triethylamine. TLC (petroleum ether/EtOAc, 1:1) of the reaction mixture after 1 h stirring at room temp. showed the complete disappearance of compound **33** ($R_f$ = 0.25) and the major formation of the expected monoacetate **35** ($R_f$ = 0.37), its 4′-*O*-acetylated regioisomer and diacetylated compound ($R_f$ = 0.53 and $R_f$ = 0.58), together with a tiny amount of a 4′-*O*-acetylated-2′,6′-lactone ($R_f$ = 0.73, ESI MS calcd. for $C_{38}H_{41}N_3NaO_{11}$ [M + Na]: 738.3; found 738.3). Purification by flash chromatography (petroleum ether/EtOAc, 1:1) and recycling as described above gave a 70% combined yield of **35** (149 mg). IR (thin film, $cm^{-1}$): $\tilde{\nu}$ = 3569, 3503, 3348 ($\nu_{O-H}$), 3080, 3064, 3032 ($\nu_{C-H,arom}$), 2955, 2924, 2854 ($\nu_{C-H,aliph}$), 2108 ($\nu_{N3}$), 1741 ($\nu_{C=O}$), 1498, 1456, 1376, 1216, 1159, 1104, 1042. $^1$H NMR (360 MHz, $CDCl_3$, ppm): δ = 7.42−7.25 (m, 10 H, Ph), 5.95 (dddd, $J_{b,ct}$ = 17.0, $J_{b,cc}$ = 10.0, $J_{b,a'}$ = 6.0, $J_{b,a}$ = 5.0 Hz, 1 H, H-b), 5.35 (dq, $J_{ct,b}$ = 17.0, $J_{ct,a}$ = $J_{ct,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-ct), 5.25 (dq, $J_{cc,b}$ = 10.0, $J_{cc,a}$ = $J_{cc,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-cc), 5.13 (br. s, 1 H, 1′-H), 4.98 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.96 (dt, $J_{2'-3'}$ = 3.0, $J_{2',1'}$ = $J_{2',4'}$ = 1.0 Hz, 1 H, 2′-H), 4.91 (d, $J_{5',4'}$ = 2.0 Hz, 1 H, 5′-H), 4.73 (d, *J* = 11.5 Hz, 1 H, C$H_2$Ph), 4.70 (d, *J* = 11.5 Hz, 1 H, C$H_2$Ph), 4.64 (d, *J* = 11.5 Hz, 1 H, C$H_2$Ph), 4.63 (d, *J* = 11.5 Hz, 1 H, C$H_2$Ph), 4.57 (d, *J* = 12.0 Hz, 1 H, C$H_2$Ph), 4.51 (d, *J* = 12.0 Hz, 1 H, C$H_2$Ph), 4.21 (ddt, $J_{gem}$ = 13.0, $J_{a,b}$ = 5.0, $J_{a,cc}$ = $J_{a,ct}$ = 1.5 Hz, 1 H, H-a), 4.05 (ddt, $J_{gem}$ = 13.0, $J_{a',b}$ = 6.0, $J_{a',cc}$ = $J_{a',ct}$ = 1.5 Hz, 1 H, H-a′), 4.04 (t, $J_{4,5}$ = $J_{4,3}$ = 9.5 Hz, 1 H, 4-H), 3.93 (br. d, $J_{4',OH}$ = 10.0 Hz, 1 H, became a ddd when an exchange with $D_2O$ was performed, $J_{4',3'}$ = 2.5, $J_{4',5'}$ = 2.0, $J_{4',2'}$ = 1.0 Hz, 4′-H), 3.84 (dd, $J_{3,2}$ = 10.0, $J_{3,4}$ = 9.5 Hz, 1 H, 4-H), 3.83 (ddd, $J_{5,4}$ = 9.5, $J_{5-6a}$ = 3.0, $J_{5,6b}$ = 2.0 Hz, 1 H, 5-H), 3.76 (dd, $J_{6a,6b}$ = 11.0, $J_{6a,5}$ = 3.0 Hz, 1 H, 6-H$^a$), 3.73 (ddd, $J_{3',2'}$ = 3.0, $J_{3',4'}$ = 2.5, $J_{3',1'}$ = 1.0 Hz, 1 H, 3′-H), 3.65 (dd, $J_{6b,6a}$ = 11.0, $J_{6b,5}$ = 2.0 Hz, 1 H, 6-H$^b$), 3.43 (dd, $J_{2,3}$ = 10.0, $J_{2,1}$ = 3.5 Hz, 1 H, 2-H), 3.38 (s, 3 H, OMe), 2.67 (d, $J_{OH,4'}$ = 10.0 Hz, 1 H, OH), 2.04 (s, 3 H, C$H_3$ OAc). $^{13}$C NMR (62.5 MHz, $CDCl_3$, ppm): δ = 169.4, 169.2 (C=O), 137.9, 137.8, 137.2 ($C_{quaternary,arom}$), 133.2 (C-b), 128.5, 128.3, 128.1, 128.0, 127.5, 127.1 ($C_{arom}$), 118.0 (C-c), 97.6 (C′-1), 96.6 (C-1), 78.4, 74.7, 74.3, 74.1 (*C*$H_2$Ph), 73.2 (*C*$H_2$Ph), 72.1 (*C*$H_2$Ph), 70.9, 68.5 (C-a), 68.1, 67.8, 67.0 (C-6), 63.5 (C-2), 51.9 (*C*$H_3$, COOMe), 20.9 (*C*$H_3$, OAc). ESI HR-MS calcd. for $C_{39}H_{45}N_3NaO_{12}$ [M + Na]: 770.29009; found 770.29063.

**Allyl (Methyl 2-*O*-acetyl-3-*O*-benzyl-4-*O*-(4-methoxybenzyl)-α-L-idopyranosyluronate)-(1→4)-*O*-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (2):** 4-Methoxybenzyl trichloroacetimidate[66] (161 mg, 0.57 mmol, 3.0 equiv.) and $BF_3$·$Et_2O$ (0.8 M in $CH_2Cl_2$, 14 μL, 0.011 mmol, 0.6 equiv.) were added successively to a cooled (−30 °C) solution of **35** (142 mg, 1.19 mmol) in $CH_2Cl_2$ (2 mL). After one hour at −30 °C, the reaction mixture was quenched with $NEt_3$ (1 M in $CH_2Cl_2$) and the solvent was evaporated. Flash chromatography of the residue gave **2** (107 mg, 65%), together with unchanged **35** (45 mg, 32%). $[\alpha]_D^{27}$ = 34 (*c* = 1.0, $CH_2Cl_2$). IR (thin film, $cm^{-1}$): $\tilde{\nu}$ = 3095, 3048, 3032, 3001 ($\nu_{C-H,arom}$), 2986, 2923, 2845 ($\nu_{C-H,aliph}$), 2108 ($\nu_{N3}$), 1736 ($\nu_{C=O}$), 1613, 1582, 1514, 1497, 1455, 1433, 1372, 1254, 1120. $^1$H NMR (250 MHz, $CDCl_3$, ppm): δ = 7.40−7.21 (m, 15 H, Ph), 7.12 (d, *J* = 8.5 Hz, 2 H, *Ph*-OMe), 6.80 (d, *J* = 8.5 Hz, 2 H, *Ph*-OMe), 5.92 (dddd, $J_{b,ct}$ = 17.0, $J_{b,cc}$ = 10.0, $J_{b,a'}$ = 6.0, $J_{b,a}$ = 5.0 Hz, 1 H, H-b), 5.33 (dq, $J_{ct,b}$ = 17.0, $J_{ct,a}$ = $J_{ct,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-ct), 5.30 (d, $J_{1',2'}$ = 4.0 Hz, 1 H, 1′-H), 5.23 (dq, $J_{cc,b}$ = 10.0, $J_{cc,a}$ = $J_{cc,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-cc), 4.94 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.89 (t, $J_{2'-3'}$ = $J_{2',1'}$ = 4.0 Hz, 1 H, 2′-H), 4.83 (d, *J* = 11.0 Hz, 1 H, C$H_2$Ph), 4.70 (d, *J* = 10.5 Hz, 1 H, C$H_2$Ph) 4.67 (d, $J_{5',4'}$ = 2.5 Hz, 1 H, 5′-H), 4.67 (d, *J* = 11.0 Hz, 1 H, C$H_2$Ph), 4.64 (d, *J* = 10.5 Hz, 1 H, C$H_2$Ph), 4.57 (d, *J* = 12.0 Hz, 1 H, C$H_2$Ph), 4.50 (d, *J* = 12.0 Hz, 1 H, C$H_2$Ph), 4.45 (d, *J* = 11.5 Hz, 1 H, C$H_2$PhOMe), 4.39 (d, *J* = 11.5 Hz, 1 H, C$H_2$PhOMe), 4.19 (ddt, $J_{gem}$ = 13.0, $J_{a,ct}$ = 5.0, $J_{a,cc}$ = $J_{a,ct}$ = 1.5 Hz, 1 H, H-a), 4.04 (t, $J_{4,3}$ = $J_{4,5}$ = 9.0 Hz, 1 H, 4-H), 4.02 (ddt, $J_{gem}$ = 13.0, $J_{a',b}$ = 6.0, $J_{a',cc}$ = $J_{a',ct}$ = 1.5 Hz, 1 H, H-a′), 3.85 (dd, $J_{3,2}$ = 10.0, $J_{3,4}$ = 9.0 Hz, 1 H, 3-H), 3.82−3.68 (m, 4 H, 5-H, 6-H$^a$, 3′-H, 4′-H), 3.78 (s, 3 H, PhO*Me*), 3.62 (dd, $J_{6b,6a}$ = 10.5, $J_{6b,5}$ = 2.0 Hz, 1 H, 6-H$^b$), 3.45 (s, 3 H, COO*Me*), 3.41 (dd, $J_{2,3}$ = 10.0, $J_{2,1}$ = 3.5 Hz, 1 H, 2-H), 1.94 (s, 3 H, C$H_3$ OAc). $^{13}$C NMR (62.5 MHz, $CDCl_3$, ppm): δ = 169.9, 169.6 (C=O), 159.3 (*C*-OMe, *p*MBn),138.1, 137.8, 137.7 ($C_{quaternary,arom}$), 133.2 (C-b), 129.5, 129.4, 128.4, 128.2, 128.0, 127.8, 127.7, 127.6, 127.5, 127.2 ($C_{arom}$), 118.0 (C-c), 113.6 ($C_m$ *p*MBn), 97.7 (C′-1), 96.5 (C-1), 78.3, 75.4, 74.7, 74.5 (*C*$H_2$Ph), 74.0, 73.3 (*C*$H_2$Ph), 72.9 (*C*$H_2$Ph), 72.3 (*C*$H_2$Ph), 70.8, 69.9, 69.6, 68.4 (C-a), 67.8 (C-6), 63.2 (C-2), 55.2 (*C*$H_3$, Ph-OMe), 51.7 (*C*$H_3$, COOMe), 20.9 (*C*$H_3$, OAc). $C_{47}H_{53}N_3O_{13}$ (867.9 g/mol): calcd. C 65.04, H 6.15, N 4.84; found C 65.28, H 6.55, N 4.39. ESI HR-MS calcd. for $C_{47}H_{53}N_3NaO_{13}$ [M + Na]: 890.34761; found 890.34797.

**Allyl 2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl-(1→4)-*O*-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (36):** Acceptor **7** (10.47 g, 23.13 mmol) was azeotropically dried with toluene. Powdered molecular sieves (4 Å, 14.86 g) and acetobromoglucose **8**[26] (23.78 g, 57.83 mmol, 2.5 equiv.) were then added, followed by

$CH_2Cl_2$ (115 mL). After 30 min stirring at room temp., the solution was cooled to −40 °C and silver triflate (14.86 g, 57.83, 2.5 mmol) was added. The reaction was then quenched with satd. aqueous $NaHCO_3$ (15 mL) after 2.5 hours at −40 °C. The reaction mixture was diluted with diethyl ether (500 mL) and filtered through a pad of Celite 545. The organic layer was washed with water (2 × 150 mL), dried ($MgSO_4$), filtered, and concentrated, giving a mixture of disaccharide **36** and excess donor **8** (30.33 g), which was generally directly deacetylated. An analytically pure sample of compound **36** was obtained by flash chromatography (toluene/EtOAc, 9:1 to 8:2). IR (thin film, $cm^{-1}$): $\tilde{\nu}$ = 3090, 3066, 3032 ($\nu_{C-H,arom}$), 2941, 2900, 2867 ($\nu_{C-H,aliph}$), 2115 ($\nu_{N3}$), 1771, 1746, 1723 ($\nu_{C=O}$), 1497, 1456, 1430, 1374, 1321, 1226, 1168. $^1$H NMR (250 MHz, $CDCl_3$, ppm): δ = 7.45−7.15 (m, 10 H, Ph), 5.91 (dddd, $J_{b,ct}$ = 17.0, $J_{b,cc}$ = 10.5, $J_{b,a'}$ = 6.0, $J_{b,a}$ = 5.0 Hz, 1 H, H-b), 5.33 (dq, $J_{ct,b}$ = 17.0, $J_{ct,a}$ = $J_{ct,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-ct), 5.23 (dq, $J_{cc,b}$ = 10.5, $J_{cc,a}$ = $J_{cc,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-cc), 5.07 (d, $J$ = 11.0 Hz, 1 H, C$H_2$Ph), 5.05−4.90 (m, 3 H, 2′-H, 3′-H, 4′-H), 4.94 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.81 (d, $J$ = 12.0 Hz, 1 H, C$H_2$Ph), 4.64 (d, $J$ = 11.0 Hz, 1 H, C$H_2$Ph), 4.47 (d, $J_{1',2'}$ = 7.5 Hz, 1 H, 1′-H), 4.43 (d, $J$ = 12.0 Hz, 1 H, C$H_2$Ph), 4.18 (ddt, $J_{gem}$ = 13.0, $J_{a,b}$ = 5.0, $J_{a,cc}$ = $J_{a,ct}$ = 1.5 Hz, 1 H, H-a), 4.14 (dd, $J_{6a',6b'}$ = 12.5, $J_{6a',5'}$ = 4.0 Hz, 1 H, 6′-H$^a$), 4.03 (ddt, $J_{gem}$ = 13.0, $J_{a',b}$ = 6.0, $J_{a',cc}$ = $J_{a',ct}$ = 1.5 Hz, 1 H, H-a′), 4.02 (t, $J_{4,5}$ = $J_{4,3}$ = 9.0 Hz, 1 H, 4-H), 3.88 (dd, $J_{6b',6a'}$ = 12.5, $J_{6b',5'}$ = 2.5 Hz, 1 H, 6′-H$^b$), 3.88 (dd, $J_{3,2}$ = 10.0, $J_{3,4}$ = 9.0 Hz, 1 H, 3-H), 3.81 (dd, $J_{6a,6b}$ = 11.0, $J_{6a,5}$ = 2.5 Hz, 1 H, 6-H$^a$), 3.69 (ddd, $J_{5,4}$ = 9.0, $J_{5,6a}$ = 2.5, $J_{5,6b}$ = 1.5 Hz, 1 H, 5-H), 3.63 (dd, $J_{6b,6a}$ = 11.0, $J_{6b,5}$ = 1.5 Hz, 1 H, 6-H$^b$), 3.35 (dd, $J_{2,3}$ = 10.0, $J_{2,1}$ = 3.5 Hz, 1 H, 2-H), 3.31 (ddd, $J_{5',4'}$ = 10.0, $J_{5',6a'}$ = 4.0, $J_{5',6b'}$ = 2.5 Hz, 1 H, 5′-H), 2.01 (s, 3 H, C$H_3$ OAc), 1.99 (s, 3 H, C$H_3$ OAc), 1.97 (s, 3 H, C$H_3$ OAc), 1.94 (s, 3 H, C$H_3$ OAc); NMR $^{13}$C (62.9 MHz, $CDCl_3$, ppm): δ (ppm) 170.5, 170.1, 169.3, 168.9 (C=O), 138.3, 137.3 ($C_{quaternary,arom}$), 133.0 ($C_a$), 128.9, 128.6, 128.3, 128.0, 127.6, 127.4 ($C_{arom}$), 118.0 (C-c), 99.8 (C′-1), 96.6 (C-1), 77.7, 77.0, 74.9 (C$H_2$Ph), 73.6 (C$H_2$Ph), 72.9, 71.6, 71.4, 70.2, 68.5 (C-a), 67.9, 67.0 (C-6 or C′-6), 62.7 (C-2), 61.5 (C-6 or C′-6), 20.6, 20.5 (C$H_3$ OAc). $C_{37}H_{45}N_3O_{14}$ (755.8 g/mol): calcd. C 58.80, H 6.00, N 5.56, O 29.64; found C 58.77, H 6.07, N 5.69, O 29.59.

**Allyl β-D-Glucopyranosyl-(1→4)-*O*-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (37):** MeONa (1.87 g, 35 mmol) was added over 1 h to a solution of the crude mixture obtained above in MeOH (200 mL). The reaction mixture was then neutralised with Dowex 50X8 200 $H^+$, filtered and concentrated. The residue was diluted with EtOAc (300 mL) and washed with water (3 × 50 mL). Water was extracted with EtOAc (3 × 50 mL) and the organic layers, containing nearly pure **37**, were combined, filtered through a silicon treated filter, and concentrated. Flash chromatography of the residue (petroleum ether/EtOAc, 3:7 to 1:9) gave **37** (10.9 g, 80% from **7**). $[\alpha]_D^{29}$ = 111 ($c$ = 1, $CH_2Cl_2$). IR (thin film, $cm^{-1}$): $\tilde{\nu}$ = 3419 (3670−3100, $\nu_{O-H}$), 3088, 3064, 3031 ($\nu_{C-H,arom}$), 2912, 2881 ($\nu_{C-H,aliph}$), 2108 ($\nu_{N3}$), 1497, 1454, 1364, 1332, 1260, 1210, 1162, 1089, 1065, 1042. $^1$H NMR (250 MHz, $CDCl_3$, 1 drop $D_2O$, ppm): δ = 7.44−7.28 (m, 10 H, Ph), 5.92 (dddd, $J_{b,ct}$ = 17.0, $J_{b,cc}$ = 10.5, $J_{b,a'}$ = 6.5, $J_{b,a}$ = 5.0 Hz, 1 H, H-b), 5.34 (dq, $J_{ct,b}$ = 17.0, $J_{ct,a}$ = $J_{ct,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-ct), 5.24 (dq, $J_{cc,b}$ = 10.5, $J_{cc,a}$ = $J_{cc,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-cc), 4.97 (d, $J$ = 11.0 Hz, 1 H, C$H_2$Ph), 4.96 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.81 (d, $J$ = 11.0 Hz, 1 H, C$H_2$Ph), 4.69 (d, $J$ = 12.0 Hz, 1 H, C$H_2$Ph), 4.50 (d, $J$ = 12.0 Hz, 1 H, C$H_2$Ph), 4.41 (d, $J_{1',2'}$ = 7.0 Hz, 1 H, 1′-H), 4.18 (ddt, $J_{gem}$ = 13.0, $J_{a,b}$ = 5.0, $J_{a,cc}$ = $J_{a,ct}$ = 1.5 Hz, 1 H, H-a), 4.04 (ddt, $J_{gem}$ = 13.0, $J_{a',b}$ = 6.5, $J_{a',cc}$ = $J_{a',ct}$ = 1.5 Hz, 1 H, H-a′), 4.00 (t, $J_{4,3}$ = $J_{4,5}$ = 9.5 Hz, 1 H, 4-H), 3.95 (dd, $J_{6a,6b}$ = 11.5, $J_{6a,5}$ = 3.0 Hz, 1 H, 6-H$^a$), 3.95 (t, $J_{3,2}$ = $J_{3,4}$ = 9.5 Hz, 1 H, 3-H), 3.85 (ddd, $J_{5,4}$ = 9.5, $J_{5,6a}$ = 3.0, $J_{5,6b}$ = 2.0 Hz, 1 H, 5-H), 3.67 (dd, $J_{6b,6a}$ = 11.5, $J_{6b,5}$ = 2.0 Hz, 1 H, 6-H$^b$), 3.59 (dd, $J_{6a',6b'}$ = 12.0, $J_{6a',5'}$ = 3.0 Hz, 1 H, 6′-H$^a$), 3.44 (dd, $J_{2,3}$ = 9.5, $J_{2,1}$ = 3.5 Hz, 1 H, 2-H), 3.40 (dd, $J_{6b',6a'}$ = 12.0, $J_{6b',5'}$ = 4.0 Hz, 1 H, 6′-H$^b$), 3.40 (t, $J_{4',3'}$ = $J_{4',5'}$ = 9.5 Hz, 1 H, 4′-H), 3.35−3.20 (m, 2 H, 3′-H, 2′-H), 3.02 (ddd, $J_{5',4'}$ = 9.5, $J_{5',6b'}$ = 4.0, $J_{5',6a'}$ = 3.0 Hz, 1 H, 5′-H), without $D_2O$ there were 4 additional br. s (1 H) at δ = 3.35, 3.13, 3.00, and 2.83. $^{13}$C NMR (62.5 MHz, $CDCl_3$, ppm): δ = 138.1, 137.4 (2 $C_{quaternary,arom}$), 133.1 (C-b), 128.5, 128.4, 128.0, 127.3 ($C_{arom}$), 118.1 (C-c), 102.1 (C′-1), 96.7 (C-1), 78.7, 76.8, 76.4, 75.5, 74.9 (C$H_2$Ph), 74.3, 73.6 (C$H_2$Ph), 70.5, 70.1, 68.6 (C-a), 68.0 (C-6), 63.3 (C-2), 61.9 (C′-6). $C_{29}H_{37}N_3O_{10}$ (587.6 g/mol): calcd. C 59.27, H 6.35; found C 58.78, H 6.61.

**Allyl [4,6-*O*-(4-Methoxybenzylidene)-β-D-glucopyranosyl]-(1→4)-*O*-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (38):** Compound **37** (10.9 g, 18.50 mmol) was dried azeotropically with toluene and dissolved in acetonitrile (80 mL). 4-Methoxybenzaldehyde dimethyl acetal (5.2 mL, 37.0 mmol, 2.0 equiv.) and catalytic camphorsulfonic acid were then added. The reaction mixture was stirred for 1 hour at room temp. and then quenched by addition of a satd. aqueous $NaHCO_3$ solution (15 mL). The resulting mixture was diluted with EtOAc (500 mL) and washed with water (2 × 100 mL), filtered through a silicon-treated filter, and concentrated. Flash chromatography of the residue (petroleum ether/EtOAc, 7:3 to 1:1) gave **38** (12.50 g, 89%) as a colourless oil. $[\alpha]_D^{29}$ = 103 ($c$ = 1, $CH_2Cl_2$). IR (thin film, $cm^{-1}$): $\tilde{\nu}$ = 3462 (3670−3270, $\nu_{O-H}$), 3089, 3065, 3033, 3009 ($\nu_{C-H,arom}$), 2936, 2904, 2872, 2840 ($\nu_{C-H,aliph}$), 2108 ($\nu_{N3}$), 1617, 1584, 1519, 1497, 1455, 1383, 1366, 1305, 1251, 1210, 1172, 1046. $^1$H NMR (250 MHz, $CDCl_3$, 1 drop $D_2O$, ppm): δ = 7.44−7.28 (m, 12 H, Ph), 6.88 (d, $J$ = 8.5 Hz, 2 H, *Ph*-OMe), 5.91 (dddd, $J_{b,ct}$ = 17.0, $J_{b,cc}$ = 10.5, $J_{b,a'}$ = 6.0, $J_{b,a}$ = 5.0 Hz, 1 H, H-b), 5.37 (s, 1 H, C*H*-PhOMe), 5.33 (dq, $J_{ct,b}$ = 17.0, $J_{ct,a}$ = $J_{ct,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-ct), 5.23 (dq, $J_{cc,b}$ = 10.5, $J_{cc,a}$ = $J_{cc,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-cc), 4.96 (d, $J$ = 10.5 Hz, 1 H, C$H_2$Ph), 4.93 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.76 (d, $J$ = 10.5 Hz, 1 H, C$H_2$Ph), 4.69 (d, $J$ = 12.0 Hz, 1 H, C$H_2$Ph), 4.49 (d, $J$ = 12.0 Hz, 1 H, C$H_2$Ph), 4.48 (d, $J_{1',2'}$ = 7.0 Hz, 1 H, 1′-H), 4.17 (ddt, $J_{gem}$ = 13.0, $J_{a,b}$ = 5.0, $J_{a,cc}$ = $J_{a,ct}$ = 1.5 Hz, 1 H, H-a), 4.12−3.96 (m, 4 H), 3.94 (t, $J$ = 9.0 Hz, 1 H), 3.84 (ddd, $J_{5,4}$ = 10.0, $J_{5,6a}$ = 3.0, $J_{5,6b}$ = 1.5 Hz, 1 H, 5-H), 3.77 (s, 3 H, OMe), 3.67 (dd, $J_{6b,6a}$ = 11.0, $J_{6b,5}$ = 1.5 Hz, 1 H, 6-H$^b$), 3.53 (t, $J_{6a',6b'}$ = $J_{6a',5'}$ = 9.5 Hz, 1 H, 6′-H$^a$), 3.42 (dd, $J_{2,3}$ = 9.5, $J_{2,1}$ = 3.5 Hz, 1 H, 2-H), 3.46−3.31 (m, 3 H), 3.06 (td, $J_{5',4'}$ = $J_{5',6a'}$ = 9.5, $J_{5',6b'}$ = 3.0 Hz, 1 H, 5′-H), without $D_2O$ there were 2 additional br. s (1 H) at δ = 3.22 and 2.95. $^{13}$C NMR (62.5 MHz, $CDCl_3$, ppm): δ = 160.1 (*C*-OMe, *p*MBn), 138.2, 137.4 ($C_{quaternary,arom}$), 133.0 (C-b), 129.3, 128.5, 128.2, 127.9, 127.6, 127.5, 127.4 ($C_{arom}$), 118.1 (C-c), 113.6 ($C_m$ *p*MBn), 102.8 (O-*C*H-O or C′-1), 101.6 (O-*C*H-O or C′-1), 96.5 (C-1), 80.2, 78.7, 77.3, 74.9 (C$H_2$Ph), 73.4 (C$H_2$Ph), 73.0, 70.2, 68.4 (C-a), 68.3 (C-6), 67.8 (C′-6), 62.9 (C-2), 55.2 (C$H_3$, OMe). $C_{37}H_{43}N_3O_{11}$ (705.8 g/mol): calcd. C 62.97, H 6.14, N 5.95; found C 62.58, H 6.24, N 5.95.

**Allyl 2,3-Di-*O*-benzyl-4,6-*O*-(4-methoxybenzylidene)-β-D-glucopyranosyl-(1→4)-*O*-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (39):** NaH (60% in oil, 2.14 g, 53.5 mmol, 3.5 equiv.) was added in small portions to a cooled (0 °C) solution of compound **38** (10.8 g, 15.3 mmol) in DMF (80 mL). After 10 min, benzyl bromide (5.5 mL, 45.9 mmol, 3.0 equiv.) was added dropwise. The mixture was then stirred at room temperature until completion of the reaction. Isopropanol (15 mL) was carefully added at 0 °C, followed by water (15 mL). The resulting mixture was diluted with

$Et_2O$ (500 mL) and washed with water (2 × 100 mL). The organic layer was dried ($MgSO_4$), filtered, and then concentrated. Flash chromatography of the residue (petroleum ether/EtOAc, 95:5 to 1:1) afforded the benzylated product **39** (15.56 g, 97%), which was crystallised from $Et_2O$/petroleum ether to give 13.01 g white crystals (mp = 119−120 °C). $[\alpha]_D^{29}$ = 35 (*c* = 1, $CH_2Cl_2$). IR (KBr pellet, $cm^{-1}$): $\tilde{\nu}$ = 3087, 3066, 3032 ($\nu_{C-H,arom}$), 2909, 2868 ($\nu_{C-H,aliph}$), 2110 ($\nu_{N3}$), 1615, 1517, 1497, 1454, 1382, 1366, 1349, 1304, 1250, 1211, 1172, 1129, 1085, 1039. $^1H$ NMR (250 MHz, $CDCl_3$, ppm): δ = 7.46−7.20 (m, 22 H, Ph), 6.91 (d, *J* = 8.5 Hz, 2 H, *Ph*-OMe), 5.94 (dddd, $J_{b,ct}$ = 17.0, $J_{b,cc}$ = 10.5, $J_{b,a'}$ = 6.0, $J_{b,a}$ = 5.0 Hz, 1 H, H-b), 5.44 (s, 1 H, C*H*-PhOMe), 5.37 (dq, $J_{ct,b}$ = 17.0, $J_{ct,a}$ = $J_{ct,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-ct), 5.25 (dq, $J_{cc,b}$ = 10.5, $J_{cc,a}$ = $J_{cc,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-cc), 5.01 (d, *J* = 10.5 Hz, 1 H, C$H_2$Ph), 4.92 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.89 (d, *J* = 12.5 Hz, 1 H, C$H_2$Ph), 4.84 (d, *J* = 11.5 Hz, 1 H, C$H_2$Ph), 4.76 (d, *J* = 12.5 Hz, 1 H, C$H_2$Ph), 4.75 (d, *J* = 11.5 Hz, 1 H, C$H_2$Ph), 4.71 (d, *J* = 10.5 Hz, 1 H, C$H_2$Ph), 4.60 (d, *J* = 12.0 Hz, 1 H, C$H_2$Ph), 4.37 (d, $J_{1',2'}$ = 7.5 Hz, 1 H, 1′-H), 4.31 (d, *J* = 12.0 Hz, 1 H, C$H_2$Ph), 4.18 (ddt, $J_{gem}$ = 13.0, $J_{a,b}$ = 5.0, $J_{a,c_c}$ = $J_{a,ct}$ = 1.5 Hz, 1 H, H-a), 4.13−3.98 (m, 3 H), 3.89 (t, *J* = 9.5 Hz, 1 H), 3.89 (dd, $J_{6b,6a}$ = 11.0, $J_{6,5}$ = 2.0 Hz, 1 H, 6-H), 3.78 (s, 3 H, OMe), 3.67 (dt, $J_{5,4}$ = 10.0, $J_{5,6a}$ = $J_{5,6b}$ = 2.0 Hz, 1 H, 5-H), 3.61−3.50 (m, 2 H), 3.50−3.30 (m, 3 H), 3.42 (dd, $J_{2,3}$ = 10.0, $J_{2,1}$ = 3.5 Hz, 1 H, 2-H), 3.08 (td, $J_{5',4'}$ = $J_{5',6a'}$ = 9.0, $J_{5',6a'}$ = 5.0 Hz, 1 H, 5′-H). $^{13}C$ NMR (62.5 MHz, $CDCl_3$, ppm): δ = 159.9 (*C*-OMe, *p*MBn), 138.3, 138.2, 137.6 ($C_{quaternary,arom}$), 133.2 (C-b), 129.7, 128.4, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.5, 127.2 ($C_{arom}$), 117.9 (C-c), 113.4 ($C_m$ *p*MBn), 102.6 (O-*C*H-O or C′-1), 100.9 (O-*C*H-O or C′-1), 96.4 (C-1), 82.3, 81.5, 80.8, 78.1, 76.7, 75.4 (*C*$H_2$Ph), 75.0 (*C*$H_2$Ph), 74.7 (*C*$H_2$Ph), 73.2 (*C*$H_2$Ph), 70.5, 68.4 (C-a and C-6 or C′-6), 67.2 (C-6 or C′-6), 65.6, 62.5 (C-2), 55.1 (*C*$H_3$, Ph-OMe). $C_{51}H_{55}N_3O_{11}$ (886.0 g/mol): calcd. C 69.14, H 6.26, N 4.74, O 19.86; found C 69.25, H 6.36, N 4.57, O 19.62.

**Allyl 2,3-Di-*O*-benzyl-4-*O*-(4-methoxybenzyl)-β-D-glucopyranosyl-(1→4)-*O*-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (40):** Triethylsilane (850 μL, 5.29 mmol, 5 equiv.) and molecular sieves (4 Å, 400 mg) were added to a solution of **39** (938 mg, 1.06 mmol) in diethyl ether (10 mL). After 30 min stirring at room temp., the solution was cooled down to −78 °C and dichlorophenylborane (740 μL, 3.6 mmol, 3.4 equiv.) was added quickly, in order to avoid freezing in the needle. The reaction mixture was warmed up to −40 °C over one hour and stirred at this temperature for one night. The reaction was then quenched at −40 °C by addition of $NEt_3$ (1.15 mL, 7.8 equiv.) and MeOH (740 μL) followed by a satd. aqueous $NaHCO_3$ solution (6 mL). The resulting suspension was filtered through a Celite 545 pad. The organic layer was then washed with an aqueous sodium hydroxide solution (0.5 M, 2 × 10 mL), aqueous 5% $KH_2PO_4$ (10 mL), and water (2 × 10 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated. Flash chromatography of the residue (petroleum ether/EtOAc, 9:1 to 7:3) gave **40** (883 mg, 91%) as a colourless oil. $[\alpha]_D^{29}$ = 63 (*c* = 1, $CH_2Cl_2$). IR (thin film, $cm^{-1}$): $\tilde{\nu}$ = 3583, 3466 ($\nu_{O-H}$), 3088, 3064, 3031, 3014 ($\nu_{C-H,arom}$), 2909, 2859 ($\nu_{C-H,aliph}$), 2107 ($\nu_{N3}$), 1737, 1612, 1586, 1514, 1497, 1454, 1361, 1304, 1249, 1210, 1067. $^1H$ NMR (250 MHz, $CDCl_3$, ppm): δ = 7.42−7.21 (m, 20 H, Ph), 7.17 (d, *J* = 8.5 Hz, 2 H, *Ph*-OMe), 6.84 (d, *J* = 8.5 Hz, 2 H, *Ph*-OMe), 5.94 (dddd, $J_{b,ct}$ = 17.0, $J_{b,cc}$ = 10.5, $J_{b,a'}$ = 6.0, $J_{b,a}$ = 5.5 Hz, 1 H, H-b), 5.36 (dq, $J_{ct,b}$ = 17.0, $J_{ct,a}$ = $J_{ct,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-ct), 5.25 (dq, $J_{cc,b}$ = 10.5, $J_{cc,a}$ = $J_{cc,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-cc), 5.01 (d, *J* = 11.0 Hz, 1 H, C$H_2$Ph), 4.94 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.88 (d, *J* = 11.0 Hz, 1 H, C$H_2$Ph), 4.82 (d, *J* = 11.0 Hz, 1 H, C$H_2$Ph), 4.81 (d, *J* = 11.0 Hz, 1 H, C$H_2$Ph), 4.79 (d, *J* = 11.0 Hz, 1 H, C$H_2$Ph), 4.75 (d, *J* = 11.0 Hz, 1 H, C$H_2$Ph), 4.71 (d, *J* = 10.5 Hz, 1 H, C$H_2$Ph), 4.58 (d, *J* = 12.0 Hz, 1 H, C$H_2$PhOMe), 4.49 (d, *J* = 10.5 Hz, 1 H, C$H_2$Ph), 4.38 (d, *J* = 12.0 Hz, 1 H, C$H_2$PhOMe), 4.34 (d, $J_{1',2'}$ = 8.0 Hz, 1 H, 1′-H), 4.19 (ddt, $J_{gem}$ = 13.0, $J_{a,b}$ = 5.5, $J_{a,cc}$ = $J_{a,ct}$ = 1.5 Hz, 1 H, H-a), 4.04 (ddt, $J_{gem}$ = 13.0, $J_{a',b}$ = 6.0, $J_{a',cc}$ = $J_{a',ct}$ = 1.5 Hz, 1 H, H-a′), 3.99 (t, $J_{4,3}$ = $J_{4,5}$ = 9.5 Hz, 1 H, 4-H), 3.89 (t, $J_{3,2}$ = $J_{3,4}$ = 9.5 Hz, 1 H, 3-H), 3.82 (dd, $J_{6a,6b}$ = 11.0, $J_{6a,5}$ = 2.0 Hz, 1 H, 6-H[a]), 3.80 (s, 3 H, OMe), 3.69 (dt, $J_{5,4}$ = 9.5, $J_{5,6a}$ = $J_{5,6b}$ = 2.0 Hz, 1 H, 5-H), 3.56 (ddd, $J_{6a',6b'}$ = 12.0, $J_{6a',OH}$ = 7.0, $J_{6a',5'}$ = 2.0 Hz, 1 H, simplified as a dd by exchange with $D_2O$, 6′-H[a]), 3.47 (dd, $J_{6b,6a}$ = 11.0, $J_{6b,5}$ = 2.0 Hz, 1 H, 6-H[b]), 3.46 (t, $J_{3',2'}$ = $J_{3',4'}$ = 8.5 Hz, 1 H, 3′-H), 3.42 (dd, $J_{2,3}$ = 9.5, $J_{2,1}$ = 3.5 Hz, 1 H, 2-H), 3.38 (t, $J_{4',3'}$ = $J_{4',5'}$ = 8.5 Hz, 1 H, 4′-H), 3.33 (dd, $J_{2',3'}$ = 8.5, $J_{2',1'}$ = 8.0 Hz, 1 H, 2′-H), 3.20 (ddd, $J_{6b',6a'}$ = 12.0, $J_{6b',OH}$ = 7.0, $J_{6b',5}$ = 5.0 Hz, simplified as a dd by exchange with $D_2O$, 1 H, 6′-H[b]), 3.08 (ddd, $J_{5',4'}$ = 8.5, $J_{5',6b'}$ = 5.0, $J_{5',6a'}$ = 2.0 Hz, 1 H, 5′-H), 1.32 (t, $J_{OH,6a'}$ = $J_{OH,6b'}$ = 7.0 Hz, OH). $^{13}C$ NMR (62.5 MHz, $CDCl_3$, ppm): δ = 159.3 (*C*-OMe, *p*MBn), 138.4, 138.3, 138.2, 137.5 ($C_{quaternary,arom}$), 133.2 (C-b), 130.1, 129.6, 128.4, 128.3, 128.2, 128.0, 127.8, 127.7, 127.6, 127.5, 127.1 ($C_{arom}$), 118.0 (C-c), 113.8 ($C_m$ *p*MBn), 102.5 (C′-1), 96.6 (C-1), 84.6, 82.7, 78.2, 77.6, 76.9, 75.6 (*C*$H_2$Ph), 75.0 (*C*$H_2$Ph), 74.9, 74.8 (*C*$H_2$Ph), 74.4 (*C*$H_2$Ph), 73.3 (*C*$H_2$Ph), 70.6, 68.5 (C-a), 67.2 (C-6), 62.9 (C-2), 61.8 (C′-6), 55.2 (*C*$H_3$, Ph-OMe). $C_{51}H_{57}N_3O_{11}$ (888.0 g/mol): calcd. C 68.98, H 6.47, N 4.73; found C 69.08, H 6.42, N 4.25.

**Allyl [Methyl 2,3-Di-*O*-benzyl-4-*O*-(4-methoxybenzyl)-β-D-glucopyranosyluronate]-(1→4)-*O*-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (3):** DMSO (474 μL, 6.67 mmol, 12 equiv.) was added dropwise to a cooled (−78 °C) solution of oxalyl chloride (160 μL, 1.67 mmol, 3 equiv.) in $CH_2Cl_2$ (5 μL). After the mixture had been kept for 15 min at −78 °C, a solution of compound **40** (474 mg, 0.56 mmol) in $CH_2Cl_2$ (500 μL) was added and the mixture was stirred for 45 minutes at −78 °C. $NEt_3$ (930 μL, 6.67 mmol, 12 equiv.) was then added dropwise over 5 min. The reaction was monitored by TLC (petroleum ether/EtOAc, 7:3. After dipping the plates into an *n*$BuNH_2$ solution (5% vol. in $CH_2Cl_2$) to allow differentiation between **40** and the aldehyde). The reaction mixture was slowly warmed to −20 °C over 1 hour and quenched with aqueous $KH_2PO_4$ (5%, 10 mL). The resulting mixture was then diluted with $Et_2O$ (100 mL) and decanted. The organic layer was washed with water (2 × 30 mL), dried ($MgSO_4$), filtered, and concentrated. The $^1H$ and $^{13}C$ NMR spectra of the crude aldehyde contain signals corresponding to the aldehyde proton (δ = 8.95 ppm, d, *J* = 1.5 Hz) and carbon (δ = 196.9 ppm). Methanolic $I_2$ (0.4 M, 4.2 mL, 1.68 mmol, 3 equiv.) and methanolic KOH (0.8 M, 4.2 mL, 3.36 mmol, 6 equiv.) were then added dropwise to a cooled (0 °C) solution of the crude aldehyde in MeOH (3 mL) as described.[17][70] After 1 h stirring at 0 °C the reaction was neutralised with methanolic AcOH (1 M), and a satd. aqueous $Na_2S_2O_3$ solution was then added until decolouration. The reaction mixture was diluted with diethyl ether (100 mL) and washed with a satd. aqueous $NaHCO_3$ solution (30 mL) and water (2 × 30 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated. Flash chromatography of the residue (petroleum ether/EtOAc, 8:2 to 7:3) gave **3** (405 mg, 79%) as a colourless oil. $[\alpha]_D^{29}$ = 54 (*c* = 1, $CH_2Cl_2$). IR (thin film, $cm^{-1}$): $\tilde{\nu}$ = 3089, 3064, 3031, 3006 ($\nu_{C-H,arom}$), 2955, 2913, 2863 ($\nu_{C-H,aliph}$), 2109 ($\nu_{N3}$), 1751 ($\nu_{C=O}$), 1716, 1613, 1586, 1514, 1497, 1454, 1361, 1303, 1250, 1217. $^1H$ NMR (250 MHz, $CDCl_3$, ppm): δ = 7.50−7.20 (m, 20 H, Ph), 7.15 (d, *J* = 8.5 Hz, 2 H, *Ph*-OMe), 6.84 (d, *J* = 8.5 Hz, 2 H, *Ph*-OMe), 5.94 (dddd, $J_{b,ct}$ = 17.0, $J_{b,cc}$ = 10.5, $J_{b,a'}$ = 6.0, $J_{b,a}$ = 5.5 Hz, 1 H, H-b), 5.35

(dq, $J_{ct,b}$ = 17.0, $J_{ct,a}$ = $J_{ct,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-ct), 5.25 (dq, $J_{cc,b}$ = 10.5, $J_{cc,a}$ = $J_{cc,a'}$ = $J_{gem}$ = 1.5 Hz, 1 H, H-cc), 5.13 (d, $J$ = 10.0 Hz, 1 H, C$H_2$Ph), 4.92 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.86 (d, $J$ = 11.0 Hz, 1 H, C$H_2$Ph), 4.80 (d, $J$ = 11.0 Hz, 1 H, C$H_2$Ph), 4.77 (s, 2 H, C$H_2$Ph), 4.69 (d, $J$ = 10.5 Hz, 1 H, C$H_2$Ph), 4.62 (d, $J$ = 12.0 Hz, 1 H, C$H_2$Ph), 4.61 (d, $J$ = 10.0 Hz, 1 H, C$H_2$PhOMe), 4.52 (d, $J$ = 10.5 Hz, 1 H, C$H_2$Ph), 4.41 (d, $J_{1',2'}$ = 7.5 Hz, 1 H, 1′-H), 4.36 (d, $J$ = 12.0 Hz, 1 H, C$H_2$PhOMe), 4.17 (ddt, $J_{gem}$ = 13.0, $J_{a,b}$ = 5.5, $J_{a,cc}$ = $J_{a,ct}$ = 1.5 Hz, 1 H, H-a), 4.06 (dd, $J_{4,5}$ = 10.0, $J_{4,3}$ = 8.5 Hz, 1 H, 4-H), 4.03 (ddt, $J_{gem}$ = 13.0, $J_{a',b}$ = 6.0, $J_{a',cc}$ = $J_{a',ct}$ = 1.5 Hz, 1 H, H-a′), 3.88 (dd, $J_{6a,6b}$ = 11.0, $J_{6a,5}$ = 2.0 Hz, 1 H, 6-H[a]), 3.87 (dd $J_{3,2}$ = 10.0, $J_{3,4}$ = 8.5 Hz, 1 H, 3-H), 3.81 (dd, $J_{4',5'}$ = 10.0, $J_{4',3'}$ = 9.0 Hz, 1 H, 4′-H), 3.78 (s, 3 H, PhO*Me*), 3.71 (dt, $J_{5',4'}$ = 10.0, $J_{5',6a'}$ = $J_{5',6b'}$ = 2.0 Hz, 1 H, 5′-H), 3.65 (dt, $J_{5,4}$ = 10.0, $J_{5,6a}$ = $J_{5,6b}$ = 2.0 Hz, 1 H, 5-H), 3.57 (s, 3 H, COO*Me*), 3.47−3.37 (m, 3 H, 2′-H, 3′-H, 6-H[b]), 3.37 (dd, $J_{2,3}$ = 10.0, $J_{2,1}$ = 3.5 Hz, 1 H, H-2). $^{13}$C NMR (62.5 MHz, $CDCl_3$, ppm): δ = 168.7 (C=O), 159.2 (*C*-OMe, *p*MBn), 138.3, 138.2, 138.1, 137.6 ($C_{quaternary,arom}$), 133.3 (C-b), 130.0, 129.5, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5 ($C_{arom}$), 117.9 (C-c), 113.7 ($C_m$ *p*MBn), 102.7 (C′-1), 96.7 (C-1), 83.8, 82.1, 79.2, 78.1, 77.1, 75.5 (*C*$H_2$Ph), 75.2 (*C*$H_2$Ph), 75.1, 74.5 (*C*$H_2$Ph), 74.3 (*C*$H_2$Ph), 73.3 (*C*$H_2$Ph), 70.5, 68.5 (C-a), 67.2 (C-6), 62.6 (C-2), 55.2 (*C*$H_3$, Ph-O*Me*), 52.3 (*C*$H_3$, COO*Me*). $C_{52}H_{57}N_3O_{12}$ (916.0 g/mol): calcd. C 68.18, H 6.27, N 4.59, O 20.96; found C 68.23, H 6.39, N 4.65, O 20.76.

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