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Total Synthesis of β-D-*Ido*-heptopyranosides Related to Capsular Polysaccharides of *Campylobacter jejuni* HS:4

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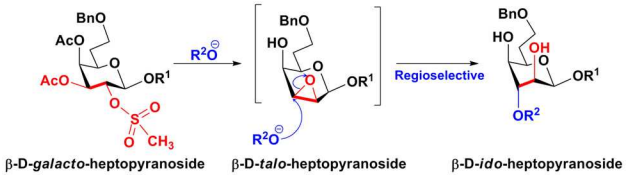

Abstract:

The 6-deoxy-β-D-*ido*-heptopyranoside related to capsular polysaccharides of *C. jejuni* HS:4 is very remarkable, owing to the unique, multifaceted structural features that have been combined into one molecule which include: (1) the rare *ido*-configuration, (2) the unusual 7-carbon backbone, and (3) the challenging β-(1→2)-*cis* anomeric configuration. Two distinct strategies toward the total synthesis of this interesting target are reported. The first involved establishment of the β-D-idopyranosyl configuration from β-D-galactopyranosides, prior to a C-6-homologation

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extending the D-hexose to the desired 6-deoxy-D-heptose. However, this approach encountered difficulties due to significantly reduced reactivity of the 6-position of the β-D-idopyranosides, so instead a second strategy was employed which involved first carrying out a 6-homologation on the less flexible D-galactopyranose, followed by a very successful conversion to the desired β-D-*ido*-configuration found in the target heptopyranoside (**2**). This report is the first successful synthesis of the 6-deoxy-β-D-*ido*-heptopyranoside which could possess interesting immunological properties.

Keywords:

Synthesis; idopyranoside; 6-homologation; 6-deoxy-β-D-*ido*-heptopyranoside; 6-deoxy-β-D-*galacto*-heptopyranoside.

1. Introduction

Campylobacter jejuni, a gram-negative, spiral-shaped bacterial pathogen, is a leading cause of bacterial infection worldwide.[1,2] The incidence of *C. jejuni* infection is extremely high, ranging from hyperendemic levels (40/100 children under 5 years old) in developing countries of the world, to endemic levels (0.2–1/100 population) in more developed regions.[4] The infection is often caused by the consumption of contaminated poultry, water, or raw milk,[5,6] and symptoms can vary from more severe (e.g. diarrhea, fever, abdominal pain), to less severe (e.g. nausea, headache, muscle pain). Although infection is not usually associated with mortality in developed countries, *C. jejuni* infection can result in a high level of morbidity. In addition, a number of post-infectious sequela can occur and can be very serious; these include the autoimmune Guillain-Barré syndrome (GBS)[7] or Miller-Fisher syndrome (MFS),[8] as well as reactive arthritis[9] among others.[10] Therefore, the development of a vaccine against *C. jejuni* infection has significant importance because of the social and economic impact of the pathogen.[11]

C. jejuni is known to produce lipooligosaccharides (LOS) which can be highly variable in structure, but often partially resemble human gangliosides.[12,13] This molecular mimicry is associated with the autoimmune disorders that are caused by *C. jejuni* infection. The bacterium also produces another class of polysaccharides, called capsular polysaccharides (CPS), which possess unique structural features. For example, **Figure 1** shows the repeating structure of *C. jejuni* serotype HS:4 (strain CG8486), the main cause of campylobacteriosis.[14] The repeating structure is a disaccharide that consists of a β-(1→3)-linked *N*-acetyl-D-glucosamine (GlcNAc) at the reducing end and a very unusual 6-deoxy-D-*ido*-heptopyranose (6-deoxy-*ido*-Hep) with β-anomeric configuration at the non-reducing end. Interestingly, partial modification with *O*-methyl phosphoramidate at the O-2 and O-7 positions of the 6-deoxy-*ido*-heptopyranose residues

was observed, resulting in heterogeneity in the isolated CPS structures. The prevalence of *C. jejuni* infection caused by HS:4 strains, as well as the unique structure of 6-deoxy-*ido*-Hep make it an ideal antigen for the development of vaccines against campylobacter infections.[15]

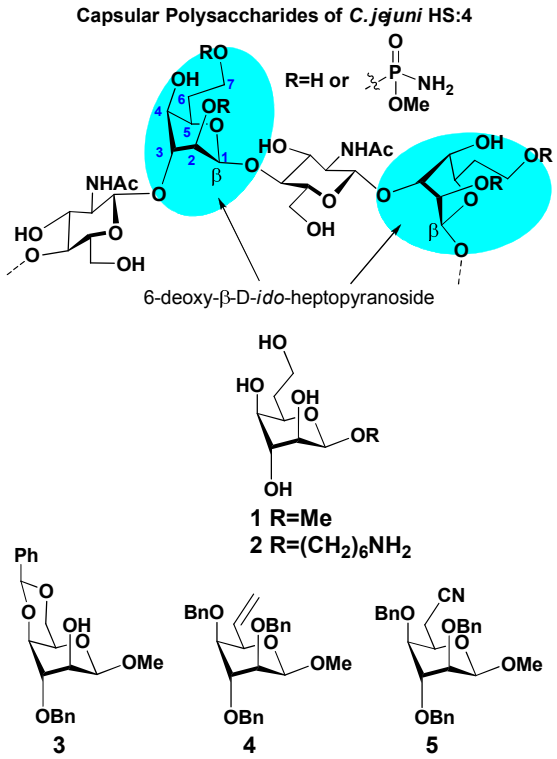


Figure 1. Structure of *C. jejuni* CPS containing an unusual 6-deoxy-β-D-*ido*-heptopyranosyl residue. Compounds **1-5** are synthetic analogs containing a β-D-idopyranosyl configuration.

Thus, 6-deoxy-*ido*-Hep derivatives such as compounds **1-2** (**Figure 1**) represent very attractive synthetic targets, but their total syntheses present a significant challenge due to their unusual 7-carbon backbone which includes a 6-deoxygenation. In addition, installation of the β-(1→2)-*cis*-anomeric configuration constitutes a well-recognized difficulty in carbohydrate chemistry. Furthermore, the *ido*-configuration which places the C-2, C-3, and C-4-hydroxyl groups in an axial position of the pyranoside $^4C_1$ chair also makes them interesting molecules to study for their unique conformational flexibility. Previously, we published a short, scalable

synthesis of compound **3** and derivatives starting from β-D-galactopyranosides, by carrying out a double inversion at both C-2 and C-3.[16-18] 2,3-Di-*O*-sulfonyl-β-D-galactopyranosides were prepared as the key substrates, and were converted to the corresponding 2,3-anhydro-β-D-talopyranoside intermediates; subsequent nucleophilic attack at C-3 by an alkoxide afforded orthogonally protected β-D-idopyranosides such as compound **3** in a single step from the 2,3-di-*O*-sulfonyl substrates. More recently, we succeeded in 6-homologation of the β-idopyranoside via Swern oxidation and Wittig olefination.[19] However, it was found that the Wittig olefination worked well only with less sterically hindered ylides such as methylenetriphenylphosphorane, to afford fully protected compound **4**. By ^{1}H NMR spectroscopy, it was observed that compound **4** preferentially adopts a $^1C_4$ chair conformation in solution, which orients the vinyl group in a more sterically hindered axial position, creating a substantial difficulty for subsequent hydroboration and preventing the desired primary alcohol from being obtained using either borane-tetrahydrofuran (THF) or 9-BBN as the reagent. We thus altered our strategy to instead focus on synthesis of the corresponding 6-nitrile derivatives, such as compound **5**, since reduction of the nitrile functionality could open an avenue to obtain the intermediate aldehyde[20] which could be further reduced to the desired 6-deoxy-*ido*-Hep (**1**).

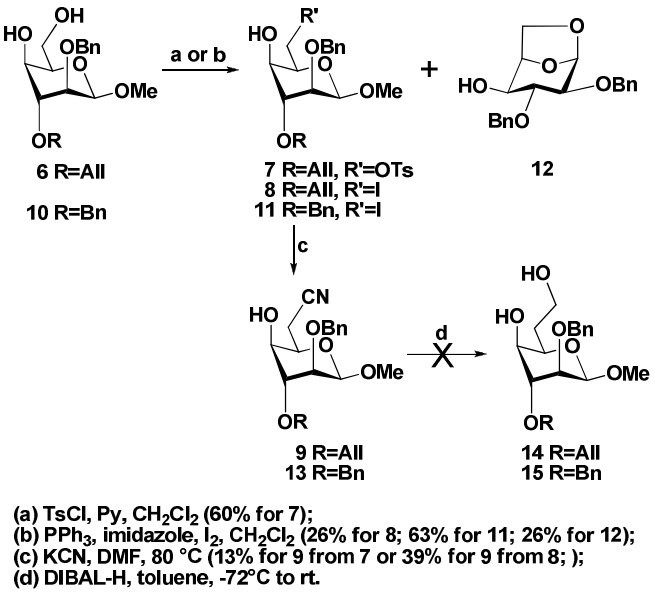
2. Results and Discussion

2.1 6-Homologation via nitrile substitution

Starting from the previously published 3-*O*-allylated β-D-idopyranoside (**6**) containing a 4,6-diol functionality, a selective O-6-tosylation was carried out in a mixture of anhydrous pyridine and dichloromethane using *p*-toluenesulfonyl chloride; this afforded regioselectively the desired 6-tosylate **7** in ~60% yield. Unfortunately, subsequent attempts at performing an S_N2 substitution with cyanide as a nucleophile in DMF at 80 °C proceeded poorly, and the best isolated yield for

desired compound **9** was only 13%. Attempts to improve the yield using either 18-crown-6 or tetra-*n*-butylammonium iodide were both unsuccessful. In fact, when 18-crown-6 was used, a small amount of hydrolyzed 6-alcohol (**6**, up to ~20%) was instead formed, likely the result of a trace amount of water present in the reagents. This was surprising to observe, given the extreme difficulty previously encountered in modifying the C-6 position directly, thus may instead result from attack of the nucleophilic H_2O (or cyanide, or both) at the S atom of the tosylate sulfonate group (as observed for the double inversion of 2,3-di-*O*-sulfonyl-β-D-galactopyranosides). Although conventionally less electrophilic, since the S center is two bonds away from the highly sterically hindered C-6 position, it should be more sterically accessible by a nucleophile.

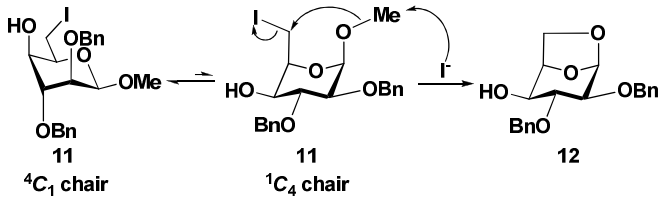
This difficulty in performing nitrile substitution at C-6 again confirmed the unusual lack of reactivity of the C-6 center in β-D-idopyranosides. We therefore decided to pursue a related substrate that instead utilized 6-iodide as the leaving group, which is known to have improved leaving group ability. Thus, starting from the same diol (**6**), a direct iodination was carried out in anhydrous dichloromethane using I_2/PPh_3 as the reagent and imidazole as base.[21, 22] Unfortunately, the iodination of compound **6** was found to be low yielding (26%), resulting from both unreacted starting material (27%) and the formation of a number of unidentified by-products as indicated by thin-layer chromatography (TLC).



Scheme 1. 6-Homologation via cyanide substitution from methyl β-D-idopyranosides **6** and **10** containing a 4,6-diol functionality.

Alternatively, we attempted to convert an analogous derivative, the 3-*O*-benzylated 4,6-diol (**10**), to the corresponding 6-iodide (**11**) as above. The reaction proceeded much better to provide compound **11** in 63% yield. Interestingly, a 1,6-anhydro by-product (**12**) was also formed from the reaction, which was isolated in 26% yield. Formation of the 1,6-anhydro by-product could be explained by an intramolecular S_N2 attack via an iodide-mediated *O*-demethylation at the anomeric position (**Scheme 2**). The β-D-idopyranosyl configuration of the substrate may promote this undesired intramolecular attack by facilitating a ring-flip to the $^1C_4$ chair conformer. Identity of the 1,6-anhydro by-product **12** was confirmed by ^{1}H NMR spectroscopy of the compound, which revealed the loss of the anomeric methyl group, as well as the presence of a hydroxyl group that correlates with H-4 in the ^{1}H-^{1}H COSY spectrum; additionally, large coupling constants were observed between H-2/H-3 and H-3/H-4 ($J_{2,3}$ = 8.0 Hz, $J_{3,4}$ = 8.1 Hz).

Furthermore, electrospray ionization high-resolution mass spectrometry (HRMS) also supported the proposed structure (calculated *m*/*z* for $[M + NH_4]^+$: 360.1805; found: 360.1802).



Scheme 2. Proposed mechanism for the formation of by-product **12**.

The iodinated intermediate **8** was then subjected to treatment with KCN in DMF at 80 °C (**Scheme 1**), but unfortunately although the substitution reaction produced higher yields than with the 6-tosylate (**7**), the isolated yield for the desired 6-nitrile **9** was still low (~40%). The transformation was observed to be quite sluggish, as large amounts of unreacted starting material were often recovered. Attempts at pushing the reaction further using excess reagent, elevated temperatures, the addition of crown ether (18-crown-6), or phase transfer catalysts (Bu_4NI) to aid in solubility were all unsuccessful. Similarly, we also attempted to carry out the displacement on compound **11** using KCN in DMF at 80 °C to obtain compound **13**. However, by TLC it was found that the expected compound **13** was formed in only low yield, and was therefore not isolated. In an effort to increase reactivity of the substrate, the 6-O-triflate was also prepared and subjected to KCN in anhydrous DMF, but unfortunately only hydrolyzed 6-alcohol (**6**) was recovered from the reaction mixture, similar to what had been observed previously during reaction of the 6-O-tosylate.

The identity of the desired product (**9**) could be confirmed by the significant shift of the ^{13}C and ^{1}H signals associated with C-6 (20.0 ppm) and H-6 (2.86 and 2.64 ppm) in the NMR spectra,

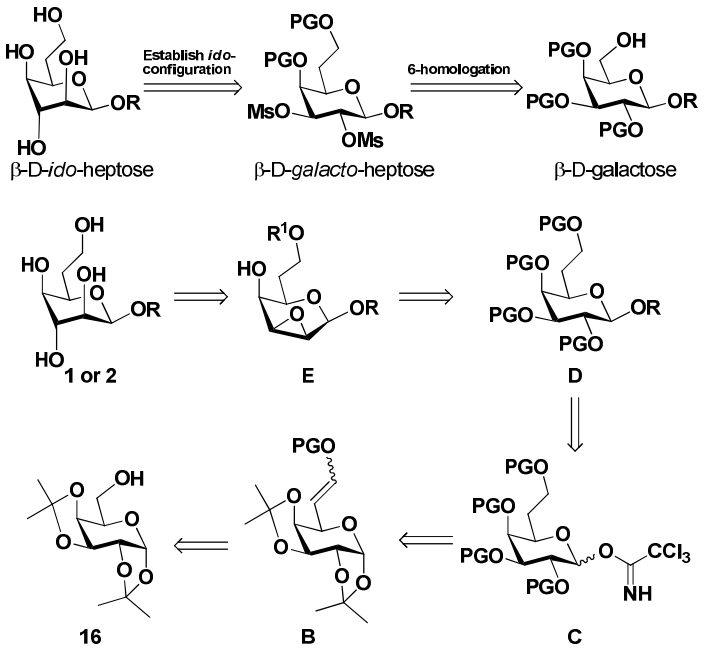
as well as confirmation via HRMS (calculated *m*/*z* for $[M + NH_4]^+$: 351.1914; found: 351.1917). Despite the poor yields of nitrile derivatives **9** and **13**, they were subsequently subjected to a reduction with DIBAL-H, as it has been well established in literature that nitrile functionalities can be reduced selectively to an intermediate aldehyde via the imine intermediate[20] and could then be further reduced to the primary alcohol (**14** or **15**). Unfortunately, all attempted reduction conditions resulted in a complex product mixture: upon purification, some unreacted starting material was isolated together with other by-products that could not be identified by ^{1}H NMR spectroscopy. Although it has been reported that in some instances DIBAL-H can cleave benzyl ether groups, this did not appear to be a major pathway of the by-product formation.[23,24]

The substantial difficulty encountered during 6-iodination and the subsequent substitution with cyanide, as well as the later reduction of the 6-nitrile functionality both appear to be consistent with the reduced reactivity of the 6-position of β-D-idopyranosides in general. Recently, we also reported an unsuccessful 6-homologation via Wittig olefination using a more sterically hindered ylide.[19] We attribute these unsuccessful chemical transformations to the unusual conformational flexibility of β-D-idopyranosides. For example, in the $^4C_1$ chair conformer, the axial substituent at C-4 sterically shields the C-6 position, while in the $^1C_4$ chair conformer, the C-6 group occupies an axial position which is inherently more sterically hindered. Thus, in either case, the functional group at the C-6 position of β-D-idopyranosides experiences reduced reactivity because of steric clashes. Previously, Streicher *et al*[25] tried to displace the 6-tosylate or 6-mesylate of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose with a cyanide, and they also encountered significant difficulty because of the steric shielding of the axial 4-substituent as is the case in our compounds (**7** and **11**); the best yield of the 6-nitrile product that they could isolate was only 4.2%, using the 6-mesylate with LiCN in DMF at 110 °C for 17

hours. We thus concluded that the successful synthesis of 6-deoxy-*ido*-Hep would require revision of our initial strategy.

2.2 Revised strategy to synthesize 6-deoxy-*ido*-heptopyranosides.

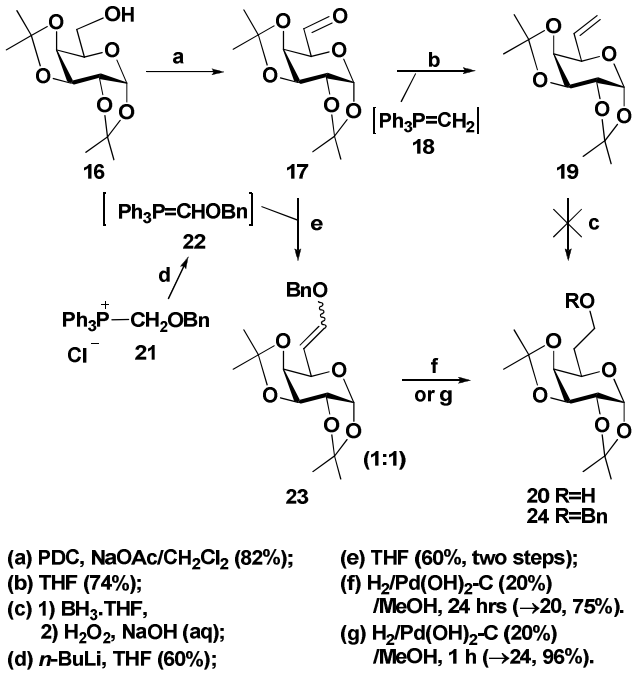
Our previous strategy provided excellent results with regards to establishing the β-(1→2)-*cis*-anomeric configuration and also the D-*ido*-configuration, but failed at 6-homologation. Thus, a logical revision of the synthetic strategy would be to reverse the steps by first completing 6-homologation on a β-D-galactopyranosyl moiety, to obtain a 6-deoxy-β-D-*galacto*-heptopyranosyl intermediate; subsequent conversion of the 6-deoxy-β-D-*galacto*-heptopyranoside to the 6-deoxy-β-D-*ido*-heptopyranoside could afford the desired target. We thought it would be advantageous to carry out the 6-homologation step on the pyranose ring of D-galactose, because of its reduced flexibility. **Scheme 3** shows the retrosynthetic route of the new strategy by using readily available 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**16**) as the starting material. We planned to attempt the 6-homologation of D-galactose by Wittig olefination to obtain structure **B**, carry out a subsequent glycosylation (structures **C** → **D**), and then finally convert the heptose from D-*galacto*- to D-*ido*-configuration via the 2,3-anhydro-*talo*-intermediate (structure **E**).



Scheme 3. A revised strategy to synthesize 6-deoxy-β-D-*ido*-heptopyranosides from D-galactopyranose by first performing the 6-homologation.

To test the feasibility of the new strategy, we first attempted to synthesize the simple 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-heptopyranose **19** via Wittig olefination (**Scheme 4**). Thus, compound **16** was first oxidized to the corresponding aldehyde **17** by pyridinium dichromate (PDC)[26] along with sodium acetate in dichloromethane, to afford the desired aldehyde in improved yield (82%). Compound **17** was then reacted with methylidenetriphenylphosphorane (**18**, $Ph_3P{=}CH_2$, generated in situ by the treatment of methyltriphenylphosphonium bromide with *n*-butyllithium, 1 equiv.) as described previously,[27] and the desired alkene **19** was successfully formed and isolated in much improved yield (74%) by column chromatography on silica gel. The structure of compound **19** was confirmed by the three vinylic protons observed at 5.94, 5.37, and 5.28 ppm. However, when alkene **19** was subjected to a hydroboration under standard reaction conditions,[28,29] no desired primary alcohol **20** was obtained. After work up, several new

compounds were indeed formed as evidenced by a number of spots observed via TLC, but upon purification none of them had the characteristic ^{1}H NMR signals corresponding to the diastereotopic protons H-6a and H-6b in the expected heptose **20**. The unsuccessful hydroboration was consistent with what has been reported previously.[19]



Scheme 4. Synthesis of 6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-heptopyranoses **20** and **24**.

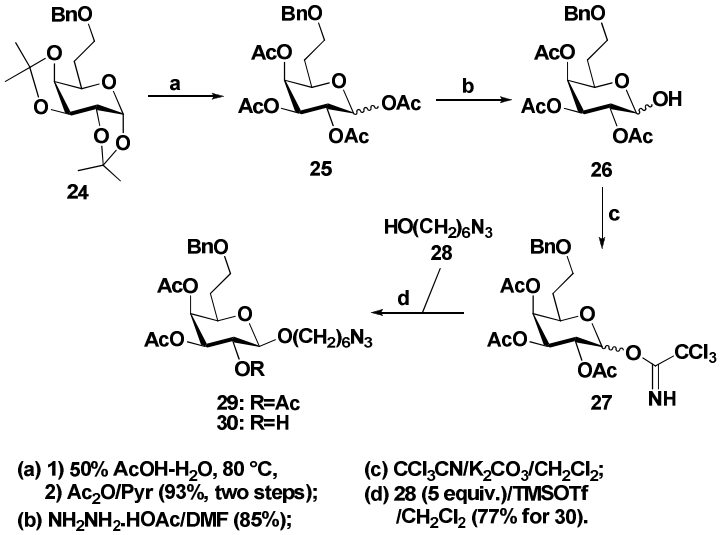
An alternative Wittig olefination with Ph_3P=CHOBn (**22**) was then carried out using again aldehyde **17**. Ylide **22** was obtained via deprotonation of the benzyloxytriphenylphosphonium salt **21** with *n*-butyllithium in THF. After stirring overnight, the desired benzylic enol ether **23** was formed and isolated in ~60% yield as a mixture of ~1:1 *E*/*Z* isomers (**Scheme 4**). Previously, Streicher *et al*[25] reported an analogous reaction using Ph_3P=CHOMe as an ylide to afford the corresponding alkenes in a similar yield. The two geometric isomers (**23E** and **23Z**) had very similar polarity. Alternatively, the E/Z mixture of benzylic enol ether **23** could be directly subjected to catalytic hydrogenation in methanol using Pearlman's catalyst; after 24

hours, the desired 6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-heptopyranose **20**[25] was obtained and isolated in 75% yield. The ^{1}H NMR spectrum of compound **20** showed two sets of multiplets at 2.00 and 1.80 ppm which are characteristic for the shielded H-6a and H-6b protons, as well as a second set of diastereotopic protons in a narrow region (3.74-3.88 ppm) which correspond to H-7a and H-7b. In the ^{1}H-^{13}C HSQC correlation spectrum, compound **20** revealed a carbon signal (C-6) at 32.8 ppm which correlated to both H-6a and H-6b, confirming the 6-deoxy functionality. In addition, a more deshielded carbon signal (C-7) at 59.9 ppm correlated to both H-7a and H-7b, confirming the presence of a hydroxyl group at C-7.

During the catalytic hydrogenation step, since two different functionalities (alkene and *O*-benzyl) were reduced concomitantly, we decided to monitor the reaction progress in order to determine whether a regioselective manipulation of the functional groups would be possible. Indeed, after subjecting the mixture to the same reaction conditions as above for only one hour, we observed the formation of a major product with an R_f of 0.64 (20% EtOAc−hexanes). The new compound was only slightly less polar than the starting materials (R_f = 0.62, 20% EtOAc−hexanes), and after stopping the reaction by a simple filtration, the newly formed product was isolated in 96% yield. To our delight, the ^{1}H NMR spectrum of the new product proved to be compound **24** (**Scheme 4**), which still had the characteristic benzylic protons at 4.55 and 4.49 ppm as two doublets (J = 11.8 Hz). In addition, two sets of proton signals were observed in a highly shielded region, 1.97 ppm (dddd, 1H, J = 13.9, 9.5, 5.3, 4.9 Hz, H-6a) and 1.90 ppm (dddd, 1H, J = 14.2, 9.8, 5.3, 4.9 Hz, H-6b), which corresponded to the diastereotopic protons H-6a and H-6b of compound **24**. As would be expected, the *E*/*Z* double bond of the benzylic enol ethers **23** preferentially reacted under hydrogenolysis conditions before cleavage of the *O*-benzyl group could occur. However, when this reaction was performed on a larger scale (>

2 g), about 20% of product **20** was still formed but could be easily *O*-benzylated again using standard alkylation conditions.

These encouraging results obtained during the 6-homologation of D-galactose prompted us to design a synthetic route to the desired 6-deoxy-β-D-*galacto*-heptopyranoside **29** from compound **24** (**Scheme 5**).



Scheme 5. Synthesis of 6-deoxy-D-*galacto*-heptopyranosyl imidate donor **27** and subsequent conversion to the corresponding heptopyranosides **29** and **30**.

The synthesis began with removal of the two isopropylidene groups of compound **24** in 50% acetic acid - water at 80 °C for 8 hours; the solution was then evaporated and treated with acetic anhydride-pyridine to afford fully acetylated intermediate **25**, isolated as an α/β-mixture in 93% yield over two steps. In order to activate the anomeric position for glycosylation, the anomeric *O*-acetate of compound **25** was regioselectively removed using hydrazinium acetate[30] in DMF (85% yield), and the obtained hemiacetal **26** was then converted to the desired *O*-trichloroacetimidate **27** by reaction with trichloroacetonitrile in dichloromethane using

anhydrous potassium carbonate as base. Since the imidate functionality is often sensitive to the mild acidity of silica gel, the crude reaction mixture was instead subjected to a quick work-up with extraction using ethyl acetate and brine, and then co-evaporated with toluene. This afforded the crude imidate **27** which was used directly for subsequent glycosylation with the previously reported 6-azidohexanol (**28**).[31] The alcohol **28** was used in excess (5 equiv.) and the glycosylation carried out at -40 °C in anhydrous dichloromethane using trimethylsilyl trifluoromethanesulfonate (TMSOTf) as a promoter in the presence of 4 Å molecular sieves;[32,33] after 4 hours, the reaction solution was warmed to ambient temperature. Surprisingly, the expected 6-azidohexyl 2,3,4-tri-*O*-acetyl-7-*O*-benzyl-6-deoxy-β-D-*galacto*-heptopyranoside **29** was not isolated, but instead an analog (**30**) which had lost the 2-*O*-acetyl group was obtained. A ^{1}H-^{1}H COSY NMR experiment (**Figure 2**) confirmed the structure of the isolated product: for example, the anomeric proton was observed as a doublet at 4.29 ppm with a large coupling constant ($J_{1,2}$ = 7.7 Hz), confirming the β-anomeric configuration. In addition, the H-2 proton was observed at 3.78 ppm as a doublet of doublets, with the lower chemical shift supporting the absence of the expected acetyl group at O-2. On the other hand, the H-3 and H-4 protons were observed at 4.96 and 5.30 ppm, respectively; both protons are significantly more deshielded than H-2, confirming the presence of an acetyl group at both O-3 and O-4. Furthermore, a very weak correlation peak was observed between H-2 and the broad peak at 2.30 ppm, which was assigned to be the hydroxyl attached to C-2. This unexpected result was indeed very beneficial to our synthesis of the final 6-deoxy-β-D-*ido*-heptopyranoside target, as the free alcohol at C-2 could be selectively activated to generate a good leaving group, which could facilitate formation of the key 2,3-anhydro intermediate (see later).

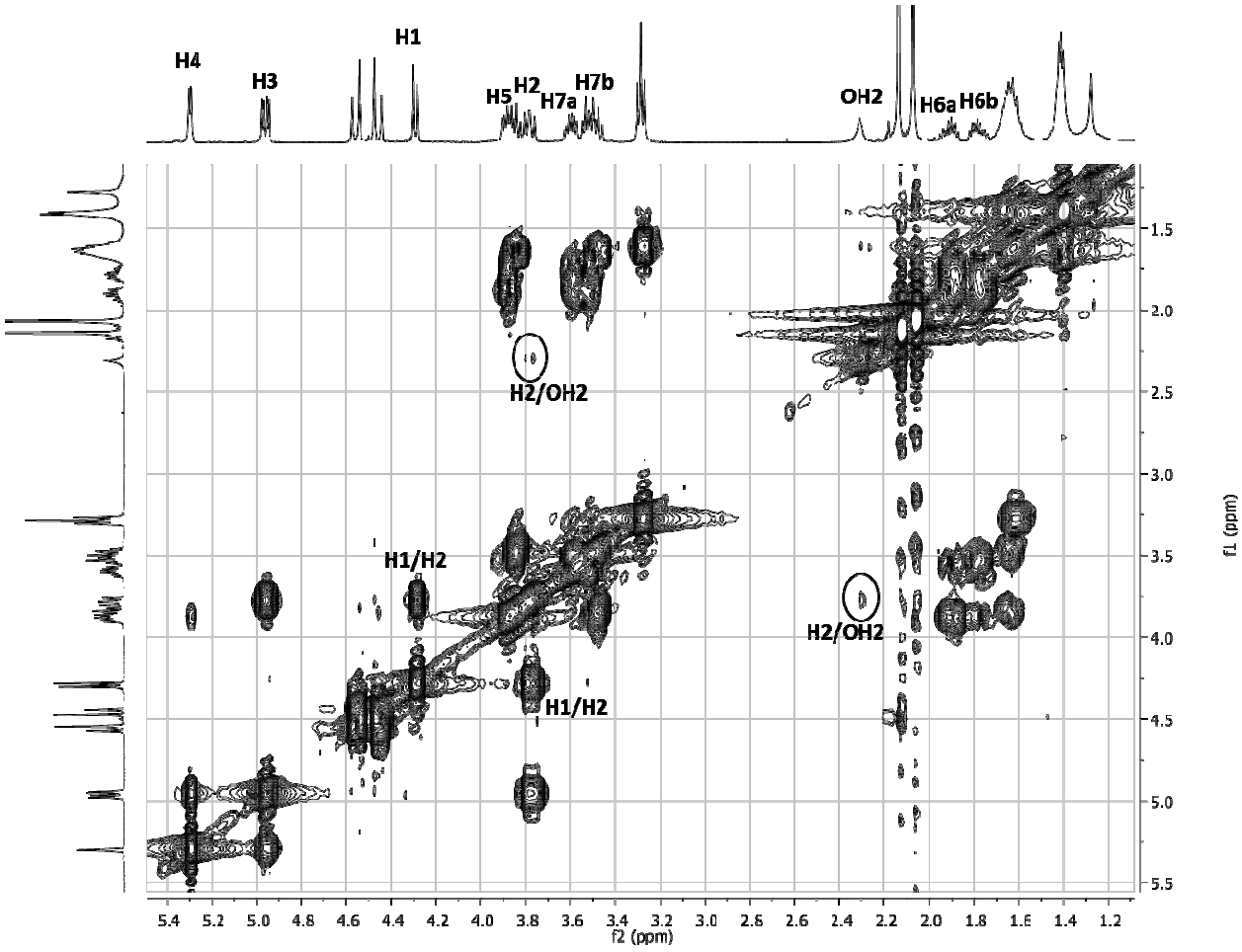
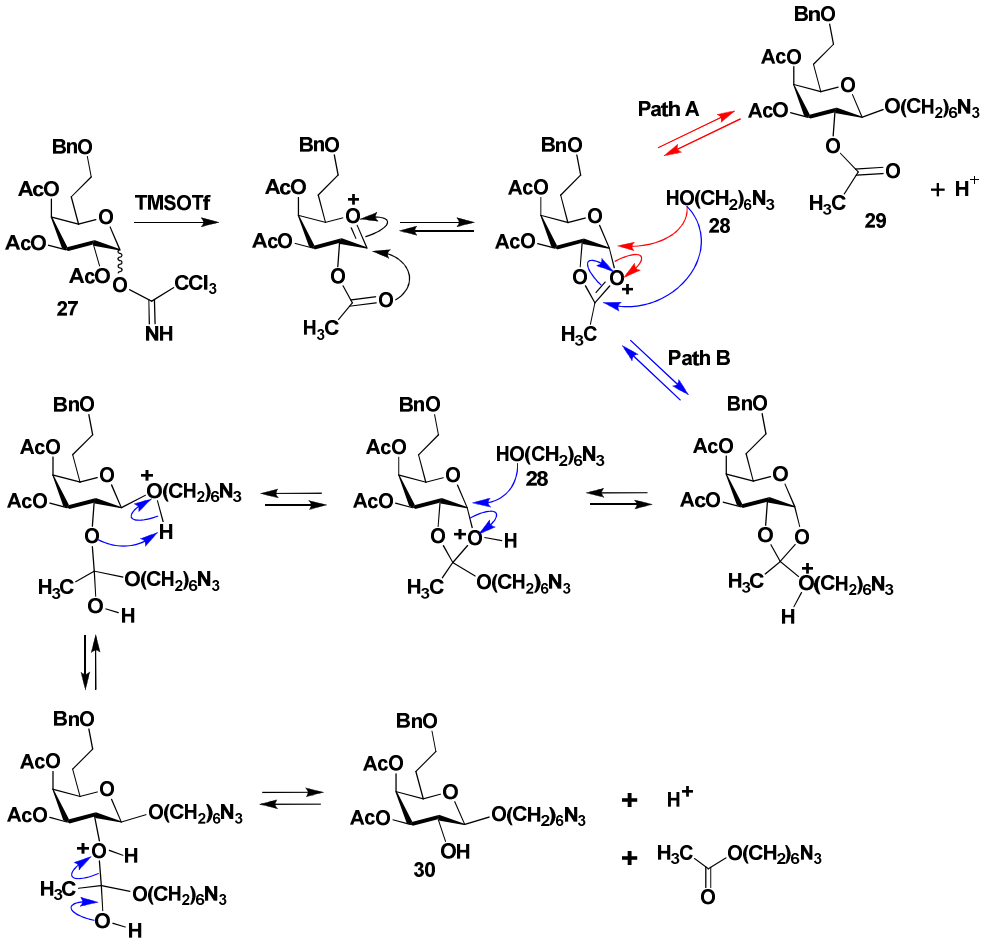


Figure 2. ^{1}H-^{1}H gCOSY spectrum of 6-azidohexyl 3,4-di-*O*-acetyl-7-*O*-benzyl-6-deoxy-β-D-*galacto*-heptopyranoside **30** ($CDCl_3$, 400 MHz, 298 K).

The reason for the regioselective loss of the 2-*O*-acetyl group could be explained by **Scheme 6**. As illustrated, after activation by TMSOTf, imidate **27** should be converted to the reactive oxocarbenium ion, which could be stabilized by participation of the O-2-acetyl group to form a bicyclic oxonium intermediate. Alcohol **28** could attack either the anomeric carbon from the top face (**Path A**) to form expected compound **29,** or the electrophilic C atom of the O-2-acetate (**Path B**) which would lead to the formation of an orthoester. After a proton transfer to the anomeric oxygen, a second molecule of alcohol **28** could attack from the top face, resulting in

the formation of the β-glycoside with an orthoacetic acid functionality which would subsequently be hydrolyzed to release the free OH-2 group and afford observed compound **30**. Previously, Nitz *et al*[34] also reported a similar 2-*O*-deacetylation when an orthoester was used as a glycosyl donor in the presence of excess allyl alcohol acceptor.



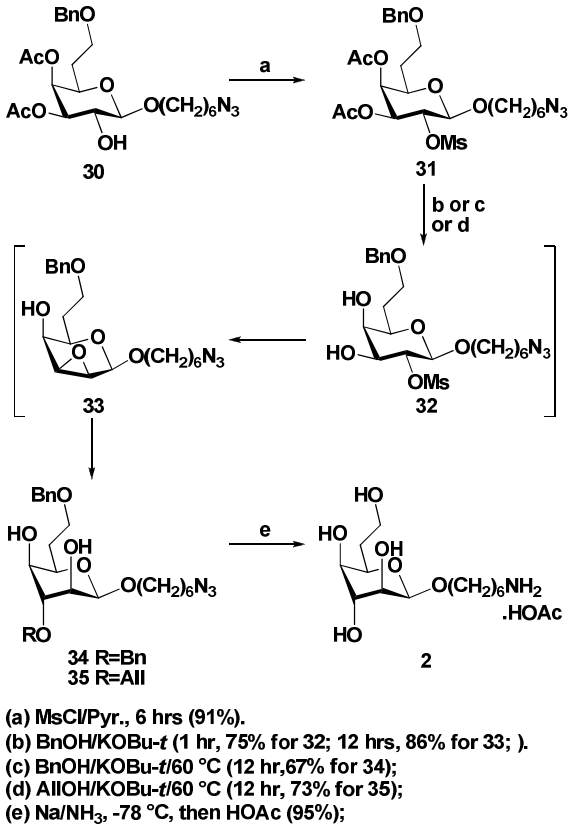
Scheme 6. A proposed pathway for the formation of 6-deoxy-β-D-*galacto*-heptopyranosides **29** and **30**.

It is worth noting that the outcome of the glycosylation reaction varied when different amounts of alcohol (**28**) were used. For example, when 1.5 equivalents of alcohol (**28**) were used

during glycosylation with imidate **27**, both the expected 2,3,4-tri-*O*-acetylated product **29** and the 2-*O*-deacetylated product **30** were obtained in a 1.7:1 ratio.

With the unexpected availability of glycoside **30**, we proceeded to activate the free OH-2 via mesylation using mesyl chloride in anhydrous pyridine, and the desired 2-*O*-mesylate **31** was isolated in 91% yield (**Scheme 7**). Compound **31** could then be directly converted into the 6-deoxy-β-D-*ido*-heptopyranoside **34** in a single step, by dissolving the mesylate **31** into benzyl alcohol and treating with potassium *tert*-butoxide: this resulted in a proton exchange between benzyl alcohol and *tert*-butoxide, affording the reactive benzyloxide which catalyzed an *O*-transesterification to remove the O-3- and O-4-acetates (→**32**). The free C-3-oxide subsequently carried out an intramolecular attack of the O-2-mesylate, to form the desired 2,3-anhydro-6-deoxy-β-D-talopyranoside intermediate (**33**). Finally, the formed 2,3-anhydro functionality was subjected to nucleophilic attack by the benzyloxide, to form the desired 3,7-di-*O*-benzylated 6-deoxy-β-D-*ido*-heptopyranoside **34**. Using 5 equivalents of potassium *tert*-butoxide and stirring at 60 °C for 10 hours successfully afforded the desired compound **34** in ~60% isolated yield. If the reaction was carried out at a lower temperature and for a shorter time, the key intermediates could instead be isolated. For example, when the reaction was carried out at ambient temperature for 1 hour, the diol **32** was isolated in 75% yield; if the reaction was quenched after 12 hours at ambient temperature, the 2,3-anhydro intermediate **33** was isolated in 86% yield. Apparently, nucleophilic opening of the anhydro functionality of compound **33** by benzyloxide proceeded very slowly at ambient temperature but could be significantly accelerated at higher temperatures (60 °C), and indeed the reaction was very regioselective to afford desired compound **34** as the only regioisomer isolated.[35]

In a similar manner, we also carried out the conversion of O-2-mesylate **31** to the related 3-*O*-allylated analog **35** in 73% yield using allyl alcohol as the solvent and nucleophile under similar conditions (**Scheme 7**).



Scheme 7. Formation of 6-deoxy-β-D-*ido*-heptopyranoside **2**.

Success in constructing the 6-deoxy-β-D-*ido*-heptopyranosyl configurations of compounds **34** and **35** was confirmed by NMR experiments based on their correlation to the unique ^{3}J coupling constants associated with the stereochemistry of β-D-*ido*-heptopyranosides. For example, for compound **34**, the anomeric proton was observed at 4.68 ppm as a doublet with a very small coupling constant ($J_{1,2}$ = 0.7 Hz); H-3 was observed at 3.91 ppm as a doublet of doublets again with small coupling constants ($J_{2,3} \approx J_{3,4} \approx$ 2.6 Hz), and H-5 was observed at 4.03 ppm as a doublet of doublets of doublets ($J_{4,5}$ < 1 Hz, $J_{5,6a}$ = 5.1 Hz, $J_{5,6b}$ = 8.2 Hz). The observation of

small coupling constants between all adjacent protons ($J_{1,2,}$ $J_{2,3,}$ $J_{3,4,}$ $J_{4,5}$) on the pyranose ring is consistent with the small dihedral angles (~60°) between adjacent protons, as expected in the $^4C_1$ *ido*-configuration of the pyranoside. On the other hand, the H-2 and H-4 protons were observed at 3.81 ppm and 3.53 ppm, respectively; analysis of their coupling patterns again afforded small coupling constants (<4.2 Hz) to neighbouring ring protons, as well as coupling to an attached hydroxyl group ($J_{2,\ OH\text{-}2}$ = 2.0 Hz; $J_{4,\ OH\text{-}4}$ could not be accurately measured due to overlapping with OCHa of the aglycone chain).

The 3,7-di-*O*-benzylated 6-deoxy-β-D-*ido*-heptopyranoside **34** was finally subjected to hydrogenolysis to remove the benzyl protecting groups and concomitantly reduce the azide functionality on the aglycone. The reaction was initially conducted in methanol using Pearlman's catalyst. However, partial *N*-methylations were observed to afford the desired compound **2** along with some *N*-methylated by-products. The *N*-methyl groups could be observed in the NMR spectrum of the crude products: for example, in the ^{1}H NMR spectrum, a singlet at 2.70 ppm and another singlet at 2.88 ppm were observed, which would correspond to *N*-methyl groups in the by-products. Electrospray-quadrupole time of flight high resolution mass spectrometry (ESI/Q-TOF HRMS) further confirmed the presence of *N*-methylated products: we observed peaks at *m*/*z* 294.1908, 308.2065, and 322.2218, which correspond respectively to the calculated *m/z* of desired product **2** ($C_{13}H_{28}NO_6$ $[M + H]^+$: 294.1911), and the mono- and di-*N*-methylated products ($C_{14}H_{30}NO_6$ $[M + H]^+$: 308.1995; $C_{15}H_{32}NO_6$ $[M + H]^+$: 322.2155). These partial *N*-methylations have also been reported recently during the catalytic hydrogenation of another family of oligosaccharide-azides.[36] Unfortunately, it was difficult to separate the partially *N*-methylated by-products from desired compound **2** which prevented them from being characterized fully.

As an alternative, a Birch reduction was adopted to concomitantly remove the benzyl groups and reduce the azide[37,38] (**Scheme 7**). The Birch reduction was carried out at -78 °C in liquid ammonia-THF using sodium metal as the reducing reagent. After one hour, the desired compound **2** was isolated as an acetic acid salt using gel filtration followed by chromatography on reverse-phase C18 silica gel using a gradient of 0→20% of methanol in water as the eluent (containing 0.2% acetic acid). **Figure 3** shows the ^{1}H-^{13}C HSQC NMR spectrum of the isolated compound **2** in D_2O. The anomeric proton (H-1) was observed at 4.72 ppm and is correlated to an anomeric carbon at 99.0 ppm. The other protons of the pyranoside ring, H-2, H-3, H-4 and H-5 protons are observed at 3.61, 3.96, 3.43 and 3.95 ppm, respectively, and they correlate with their attached carbons at 69.4 (C-2), 69.8 (C-3), 69.8 (C-4) and 71.1 (C-5) ppm, respectively. The observed vicinal coupling constants were consistently small ($J_{1,2}$ = ~1 Hz, $J_{2,3}$ = 3.5 Hz, $J_{3,4}$ = 3.5 Hz, $J_{4,5}$ = 1.9 Hz), confirming the β-(1→2)-*cis*-anomeric configuration as well as the *ido*-configuration. The two diastereotopic protons H-6a and H-6b were found in a highly shielded region (1.91 and 1.70 ppm, respectively), confirming the 6-deoxy functionality. Finally, HRMS (ESI/Q-TOF) also revealed a peak at *m/z* 294.1908 which corresponds to the calculated *m/z* 294.1911 for the expected formula of compound **2** $C_{13}H_{28}NO_6$ $[M + H]^+$.

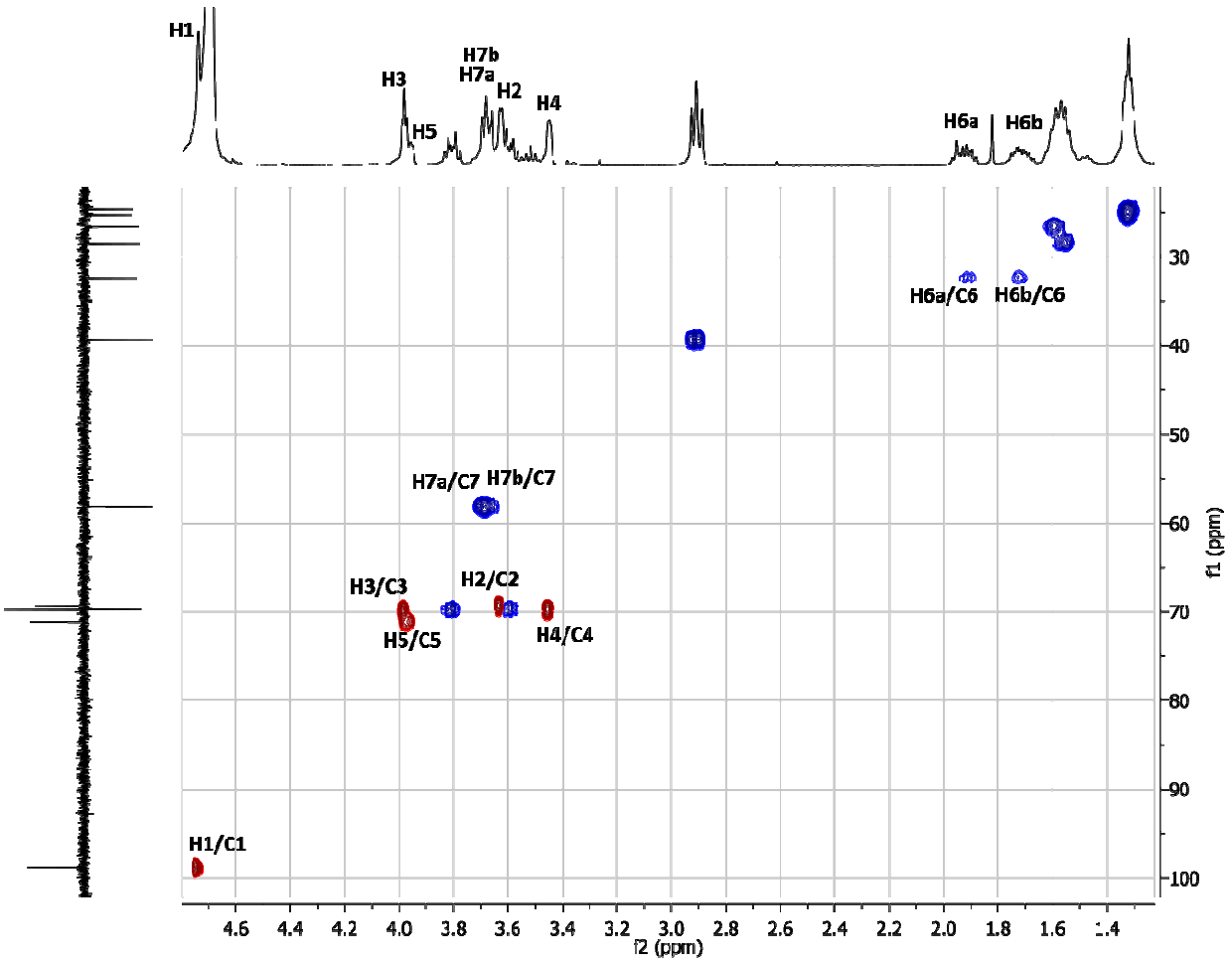


Figure 3. ^{1}H-^{13}C gHSQC spectrum of 6-deoxy-β-D-*ido*-heptopyranoside **2** (D_2O, 400 MHz, 298 K).

3. Conclusions

In conclusion, two distinct strategies have been studied to progress toward total synthesis of the challenging 6-deoxy-β-D-*ido*-heptopyranoside related to *C. jejuni* HS:4 CPS. The first strategy involved establishment of the β-D-idopyranosyl configuration from β-D-galactopyranosides prior to extending the D-hexose to the desired 6-deoxy-D-heptose via C-6-homologation. However, this approach was found to be impractical, as the C-6-position of the β-D-idopyranosides was observed to exhibit significantly reduced reactivity, probably caused by an

increased steric hindrance of the 6-position which is exacerbated by enhanced conformational flexibility of the β-D-idopyranosyl ring. The second strategy involved carrying out a 6-homologation on the less flexible D-galactopyranose to first obtain a 6-deoxy-β-D-*galacto*-heptopyranoside, followed by establishment of the β-D-*ido*-configuration in target heptopyranoside **2**. This strategy was found to be very productive, allowing for the successful synthesis of a 6-deoxy-β-D-*ido*-heptopyranoside (**2**) for the first time. In both strategies, the conversion of β-D-*galacto*-configuration to β-D-*ido*-configuration was achieved by a double inversion at the C-2 and C-3 positions via a 2,3-anhydro-β-D-*talo*-pyranosyl intermediate; opening of the 2,3-anhydro-functionality by an alkoxide was found to be very regio- and stereoselective, with nucleophilic attack occurring exclusively at the C-3 position. The overall transformation of stereochemistry was proven to be very efficient, and required minimal purification. Additionally, our strategy to synthesize β-D-idopyranosides from β-D-galactopyranosides is very versatile, as it can be successfully carried out on both hexoses and heptoses. This success in synthesis of the 6-deoxy-β-D-*ido*-heptopyranoside (**2**) should permit us to study its immunological properties in the future.

4. Experimental section

General Methods. All commercial reagents were used as supplied unless otherwise stated. Thin layer chromatography was performed on Silica Gel 60-F254 (E. Merck, Darmstadt) with detection by fluorescence, charring with 5% H_2SO_4 (aq), or a ceric ammonium molybdate solution. Column chromatography was performed on Silica Gel 60 (Silicycle, Ontario) and solvent gradients given refer to stepped gradients and concentrations are reported as % v/v.

Organic solutions were concentrated and/or evaporated to dry under vacuum in a water bath (<60 °C). Molecular sieves were stored in an oven at 100° C and flame-dried under vacuum before use. Amberlite IR-120 (H^+) ion exchange resin was washed multiple times with MeOH prior to use. All pH values were determined using universal pH paper. Optical rotations were determined in a 5 cm cell at 20 ± 2 °C; $[\alpha]_D^{20}$ values are given in units of 10^{-1} deg•cm^2/g. NMR spectra were recorded on Bruker spectrometers at 400 MHz, and the first-order chemical shifts of ^{1}H and ^{13}C (DEPT-Q) are reported in δ (ppm) and referenced to residual $CHCl_3$ (δ_H 7.24, δ_C 77.23, $CDCl_3$), or residual HDO (δ_H 4.79, external acetone δ_C 29.9, D_2O). ^{1}H and ^{13}C NMR spectra were assigned with the assistance of 2D gCOSY and 2D gHSQC experiments. High-resolution ESI-QTOF mass spectra were recorded on an Agilent 6520 Accurate Mass Quadrupole Time-of-Flight LC/MS spectrometer. Elemental analyses were obtained with a Perkin Elmer Series II 2400 CHNS/O Analyzer. All the data were obtained with the assistance of the analytical services of the Department of Chemistry, University of Calgary.

Methyl 3-O-allyl-2-O-benzyl-6-O-tosyl-β-D-idopyranoside (7): Compound **6** (481 mg, 1.48 mmol) and *p*-TsCl (318 mg, 1.67 mmol) were dissolved into dry pyridine (5.0 mL) and left mixing at rt. After 6 h additional *p*-TsCl (43 mg, 0.23 mmol) was added. After 20 h, the reaction was quenched with MeOH (5 mL), then evaporated to dry via co-evaporation with toluene (3 × 5 mL). The crude product was re-dissolved into EtOAc (100 mL), washed with saturated NaCl (aq) solution (3 × 100 mL), dried with Na_2SO_4, filtered, and evaporated to dry. The crude mixture was purified by column chromatography on silica gel using 25% acetone – hexanes to afford the desired product **7** as a colourless syrup (423 mg, 0.884 mmol, 60% yield), as well as a small amount of di-tosylated by-product. R_f 0.66 (EtOAc : hexanes 2:3). $[\alpha]_D^{20}$: -72.4° (*c* 1.02, $CHCl_3$).

^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.79 – 7.74 (m, 2H, Ar), 7.31 – 7.24 (m, 7H, Ar), 5.72 (dddd, 1H, J = 17.2, 10.4, 5.6, 5.6 Hz, $OCH_2C\underline{H}=CH_2$), 5.13 (dddd, 1H, J = 17.2, 1.6, 1.6, 1.6 Hz, $OCH_2CH=C\underline{H_a}H_b$), 5.11 (dddd, 1H, J = 10.4, 1.5, 1.3, 1.3 Hz, $OCH_2CH=CH_a\underline{H_b}$), 4.83 (d, 1H, J = 12.1 Hz, $PhC\underline{H_a}H_b$), 4.58 (d, 1H, J = 12.1 Hz, $PhCH_a\underline{H_b}$), 4.57 (d, 1H, J = 1.0 Hz, H-1), 4.24 (dd, 1H, J = 10.3, 5.1 Hz, H-6a), 4.20 (dd, 1H, J = 10.3, 6.9 Hz, H-6b), 4.02 (ddd, 1H, J = 6.7, 5.2, <1 Hz, H-5), 3.90 (dddd, 1H, J = 12.9, 5.6, 1.4, 1.4 Hz, $OC\underline{H_a}H_bCH=CH_2$), 3.86 (dddd, 1H, J = 12.9, 5.7, 1.4, 1.4 Hz, $OCH_a\underline{H_b}CH=CH_2$), 3.64 – 3.62 (m, 1H, H-3), 3.55 (dd, 1H, J = 3.4, 0.8 Hz, H-2), 3.50 – 3.48 (m, 4H, OMe and H-4), 3.42 (broad, 1H, 4-OH), 2.40 (s, 3H, Ts). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 144.9 (Ar), 137.4 (Ar), 133.8 ($OCH_2\underline{C}H=CH_2$), 132.9 (Ar), 129.9 (Ar), 128.5 (Ar), 128.2 (Ar), 128.14 (Ar), 128.06 (Ar), 117.9 ($OCH_2CH=\underline{C}H_2$), 100.8 (C-1), 75.1 (C-3), 74.4 ($Ph\underline{C}H_2$), 74.3 (C-2), 73.0 (C-5), 71.2 ($O\underline{C}H_2CH=CH_2$), 69.7 (C-6), 66.6 (C-4), 57.2 (OMe), 21.7 (Ts). HRMS (ESI-QTOF) *m/z*: $[M + Na]^+$ calcd for $C_{24}H_{30}O_8SNa$ 501.1554, found 501.1551.

*Methyl 3-O-allyl-2-O-benzyl-6-deoxy-6-iodo-β-D-idopyranoside (**8**)*: A solution of compound **6** (2.078 g, 6.405 mmol), PPh_3 (2.196 g, 8.374 mmol), and imidazole (0.800 g, 11.8 mmol) in dry CH_2Cl_2 (20 mL) was flushed with Ar, and then cooled to 0 °C in an ice-H_2O bath. I_2 (2.649 g, 10.44 mmol) was added in one portion, and the reaction mixture was slowly warmed back to ambient temperature. After 24 h, a fresh solution of PPh_3 (1.306 g, 4.978 mmol) and I_2 (1.350 g, 5.321 mmol) in dry CH_2Cl_2 (10 mL) was added to the reaction mixture. After an additional 24 h, the solution was evaporated to dry and then redissolved into EtOAc (120 mL). The organic phase was washed with saturated $Na_2S_2O_3$ (aq) solution (4 × 120 mL), dried with Na_2SO_4, filtered, and evaporated to dry. The crude material was then purified via column chromatography on silica

using 8→15→20% acetone – hexanes to afford the pure product **8** as a yellow syrup (721 mg, 1.66 mmol, 26% yield), unreacted starting material (555 mg, 1.71 mmol, 27% recovered). R_f 0.85 (EtOAc : toluene 6:4). $[\alpha]_D^{20}$: -44° (*c* 0.86, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.34 – 7.28 (m, 5H, Ar), 5.76 (dddd, 1H, *J* = 17.2, 10.4, 5.7, 5.7 Hz, $OCH_2C\underline{H}=CH_2$), 5.16 (dddd, 1H, *J* = 17.2, 1.6, 1.6, 1.6 Hz, $OCH_2CH=C\underline{H}_aH_b$), 5.13 (dddd, 1H, *J* = 10.4, 1.4, 1.4, 1.4 Hz, $OCH_2CH=CH_a\underline{H}_b$), 4.88 (d, 1H, *J* = 12.2 Hz, $PhC\underline{H}_aH_b$), 4.62 (d, 1H, *J* = 12.2 Hz, $PhCH_a\underline{H}_b$), 4.61 (d, 1H, *J* = 1.0 Hz, H-1), 3.94 – 3.90 (m, 3H, $OC\underline{H}_2CH=CH_2$ and H-5), 3.70 – 3.66 (m, 2H, H-3 and H-4), 3.60 (s, 3H, OMe), 3.53 (ddd, 1H, *J* = 3.1, 1.2, 1.2 Hz, H-2), 3.48 (dd, 1H, *J* = 12.6, 1.0 Hz, 4-OH), 3.40 (dd, 1H, *J* = 10.2, 7.7 Hz, H-6a), 3.37 (dd, 1H, *J* = 10.2, 6.2 Hz, H-6b). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 137.6 (Ar), 134.0 ($OCH_2\underline{C}H=CH_2$), 128.7 (Ar), 128.34 (Ar), 128.26 (Ar), 118.1 ($OCH_2CH=\underline{C}H_2$), 101.5 (C-1), 76.0 (C-5), 75.9 (C-3), 74.6 ($Ph\underline{C}H_2$), 74.3 (C-2), 71.4 ($O\underline{C}H_2CH=CH_2$), 67.8 (C-4), 57.4 (OMe), 4.0 (C-6). HRMS (ESI-QTOF) *m/z*: $[M + Na]^+$ calcd for $C_{17}H_{23}IO_5Na$ 457.0482, found 457.0479.

*Methyl 3-O-allyl-2-O-benzyl-6-cyano-6-deoxy-β-D-idopyranoside (**9**)*: Method A: A solution of the 6-*O*-tosyl starting material **7** (121 mg, 0.252 mmol), KCN (76 mg, 1.2 mmol), and 18-crown-6 (299 mg, 1.13 mmol) in dry DMF (1.3 mL) were left mixing at rt. After 48 h, the mixture was temperature was increased to 60 °C. After 24 h of heating, the reaction mixture was evaporated to dry, redissolved into EtOAc (50 mL), washed with saturated NaCl (aq) solution (3 × 50 mL), dried with Na_2SO_4, filtered, and evaporated to dry. The crude material was purified via column chromatography on silica using 15→25→40% EtOAc – hexanes to afford the desired product **9** as a colourless syrup (11 mg, 0.032 mmol, 13% yield), the hydrolyzed by-product **6**

(16 mg, 0.048 mmol, 19% yield). Attempts at using Bu_4NI instead of 18-crown-6 were also unsuccessful, and resulted in significant formation of the hydrolyzed by-product **6**.

Method B: Compound **8** (113 mg, 0.260 mmol) and KCN (59 mg, 0.91 mmol) were dissolved into dry DMF (1.3 mL) and left mixing at 80 °C. After 48 h, the reaction mixture was diluted with EtOAc (60 mL), washed with saturated NaCl (aq) solution (3 × 60 mL), dried with Na_2SO_4, filtered, and evaporated to dry. The crude material was purified via column chromatography on silica using 10→15→20% EtOAc – hexanes to afford the pure product as a pale yellow syrup (34 mg, 0.10 mmol, 39% yield). Attempts to leave the reaction for longer or at increased temperatures resulted in the formation of a number of uncharacterized by-products. R_f 0.56 (EtOAc : hexanes 2:3). $[\alpha]_D^{20}$: -50° (*c* 0.94, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.35 – 7.28 (m, 5H, Ar), 5.75 (dddd, 1H, *J* = 17.0, 10.5, 5.7, 5.7 Hz, $OCH_2C\underline{H}=CH_2$), 5.15 (dddd, 1H, *J* = 17.1, 1.5, 1.5, 1.5 Hz, $OCH_2CH=C\underline{H}_aH_b$), 5.14 (dddd, 1H, *J* = 10.5, 1.3, 1.3, 1.3 Hz, $OCH_2CH=CH_a\underline{H}_b$), 4.88 (d, 1H, *J* = 12.1 Hz, $PhC\underline{H}_aH_b$), 4.65 (d, 1H, *J* = 0.9 Hz, H-1), 4.62 (d, 1H, *J* = 12.1 Hz, $PhCH_a\underline{H}_b$), 4.08 (ddd, 1H, *J* = 8.6, 5.5, 1.3 Hz, H-5), 3.92 (dddd, 2H, *J* = 5.7, 1.4, 1.4, <1 Hz, $OC\underline{H}_2CH=CH_2$), 3.71 (dd, 1H, *J* = 3.3, 3.3 Hz, H-3), 3.59 (ddd, 1H, *J* = 3.4, 1.0, 1.0 Hz, H-2), 3.58 (s, 3H, OMe), 3.58 (d, 1H, *J* = 11.7 Hz, 4-OH), 3.46 (dddd, 1H, *J* = 11.6, 3.1, 1.2, 1.2 Hz, H-4), 2.86 (dd, 1H, *J* = 16.8, 8.6 Hz, H-6a), 2.64 (dd, 1H, *J* = 16.8, 5.5 Hz, H-6b). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 137.4 (Ar), 133.8 ($OCH_2\underline{C}H=CH_2$), 128.7 (Ar), 128.4 (Ar), 118.3 ($OCH_2CH=\underline{C}H_2$), 117.8 (CN), 101.2 (C-1), 75.3 (C-3), 74.7 ($Ph\underline{C}H_2$), 74.0 (C-2), 71.6 ($O\underline{C}H_2CH=CH_2$), 71.3 (C-5), 67.6 (C-4), 57.4 (OMe), 20.0 (C-6). HRMS (ESI-QTOF) *m/z*: $[M + NH_4]^+$ calcd for $C_{18}H_{27}N_2O_5$ 351.1914, found 351.1917.

*Methyl 2,3-di-O-benzyl-6-deoxy-6-iodo-β-D-idopyranoside (**11**) and 1,6-anhydro-2,3-di-O-benzyl-β-D-idopyranose (**12**)*: A solution of the compound **10** (152 mg, 0.407 mmol), PPh_3 (129 mg, 0.491 mmol), and imidazole (62 mg, 0.91 mmol) in dry CH_2Cl_2 (1.5 mL) was flushed with Ar, and then cooled to 0 °C. I_2 (170 mg, 0.671 mmol) was added in one portion, and the reaction mixture slowly warmed back to ambient temperature. After 24 h, a solution of PPh_3 (218 mg, 0.832 mmol) and I_2 (214 mg, 0.844 mmol) in CH_2Cl_2 (0.5 mL) was added at 0 °C and then the solution warmed back to ambient temperature. After another 24 h, the solution was evaporated to dry and then redissolved into EtOAc (60 mL). The organic phase was washed with saturated $Na_2S_2O_3$ (aq) solution (2 × 60 mL), saturated NaCl (aq) solution (2 × 60 mL), dried with Na_2SO_4, filtered, and evaporated to dry. The crude material was then purified via column chromatography on silica using 10→15→20% acetone – hexanes to afford the pure product **11** as a yellow syrup (124 mg, 0.257 mmol, 63% yield), the 1,6-anhydro by-product **12** (36 mg, 0.11 mmol, 26% yield). Data for **11**: R_f 0.70 (EtOAc : toluene 3:2). $[\alpha]_D^{20}$: -64° (*c* 0.96, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.36 – 7.27 (m, 8H, Ar), 7.23 – 7.19 (m, 2H, Ar), 4.85 (d, 1H, *J* = 12.2 Hz, PhC$\underline{H}_a$H$_b$), 4.67 (d, 1H, *J* = 0.9 Hz, H-1), 4.61 (d, 1H, *J* = 12.2 Hz, PhCH$_a\underline{H}_b$), 4.49 (d, 1H, *J* = 11.9 Hz, PhC$\underline{H}_a$H$_b$), 4.45 (d, 1H, *J* = 11.9 Hz, PhCH$_a\underline{H}_b$), 3.98 (ddd, 1H, *J* = 7.6, 6.3, 0.9 Hz, H-5), 3.78 (dd, 1H, *J* = 3.2, 3.2 Hz, H-3), 3.74 (dddd, 1H, *J* = 11.5, 3.1, 1.1, 1.1 Hz, H-4), 3.61 (s, 3H, OMe), 3.57 (ddd, 1H, *J* = 3.2, 1.1, 1.0 Hz, H-2), 3.50 (d, 1H, *J* = 11.6 Hz, 4-OH), 3.42 (dd, 1H, *J* = 10.1, 7.7 Hz, H-6a), 3.39 (dd, 1H, *J* = 10.2, 6.2 Hz, H-6b). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 137.5 (Ar), 137.4 (Ar), 128.7 (Ar), 128.6 (Ar), 128.22 (Ar), 128.16 (Ar), 127.8 (Ar), 101.4 (C-1), 75.92 (C-3), 75.88 (C-5), 74.4 (Ph$\underline{C}$H$_2$), 74.1 (C-2), 72.4 (Ph$\underline{C}$H$_2$), 67.6 (C-4), 57.2 (OMe), 3.9 (C-6). HRMS (ESI-QTOF) *m/z*: $[M + Na]^+$ calcd for $C_{21}H_{25}IO_5Na$ 507.0639, found 507.0642. Data for **12**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.37 – 7.26 (m, 10H, Ar), 5.32 (d, 1H, *J*

= 1.5 Hz, H-1), 4.91 (d, 1H, J = 11.6 Hz, PhC$\underline{H}_a$H$_b$), 4.69 (d, 1H, J = 11.6 Hz, PhCH$_a\underline{H}_b$), 4.68 (s, 2H, PhC$\underline{H}_2$), 4.36 (ddd, 1H, J = 4.6, 4.6, <1 Hz, H-5), 4.04 (dd, 1H, J = 7.7, <1 Hz, H-6a), 3.82 – 3.78 (m, 1H, H-4), 3.68 (dd, 1H, J = 7.7, 5.0 Hz, H-6b), 3.60 (dd, 1H, J = 8.1, 8.1 Hz, H-3), 3.49 (dd, 1H, J = 8.0, 1.6 Hz, H-2), 2.08 (d, 1H, J = 2.6 Hz, 4-OH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 138.8 (Ar), 138.1 (Ar), 128.8 (Ar), 128.7 (Ar), 128.21 (Ar), 128.16 (Ar), 128.15 (Ar), 128.1 (Ar), 99.8 (C-1), 82.8 (C-2), 82.5 (C-3), 75.24 (Ph$\underline{C}$H$_2$), 75.20 (C-5), 73.0 (Ph$\underline{C}$H$_2$), 71.5 (C-4), 65.5 (C-6). HRMS (ESI-QTOF) *m/z*: $[M + NH_4]^+$ calcd for $C_{20}H_{26}NO_5$ 360.1805, found 360.1802.

*Methyl 2,3-di-O-benzyl-6-cyano-6-deoxy-β-D-idopyranoside (**13**)*: The starting material (**11**, 630 mg, 1.30 mmol) and KCN (674 mg, 10.4 mmol) in dry DMF (10 mL) were heated at 80 °C. After 24 h the reaction was concentrated to half volume via co-evaporation with toluene (2 × 10 mL), then diluted with EtOAc (100 mL). The organic phase was washed with saturated NaCl (aq) solution (3 × 100 mL), H_2O (100 mL), dried with Na_2SO_4, filtered, and evaporated to dry. The crude material was used directly for the following step.

*Methyl 2,3-di-O-benzyl-β-D-ido-heptopyranoside (**15**):* The crude starting material **13** (1.30 mmol from previous step) was dissolved into dry toluene (20 mL), and cooled to -72 °C. DIBAL-H solution (1 M in toluene, 19 mL, 19 mmol) was added dropwise over 15 min, and after 2 h the reaction mixture slowly warmed up to ambient temperature. After 24 h, the reaction mixture was diluted with CH_2Cl_2 (20 mL) and then quenched with MeOH (30 mL). The crude mixture was evaporated to dry, then redissolved into EtOAc (100 mL), washed with 1.2 M HCl

(aq) (2 × 100 mL), H_2O (100 mL), dried with Na_2SO_4, filtered, and evaporated to dry. TLC indicated a complex mixture of products had formed, but none were successfully identified.

*1,2;3,4-Di-O-isopropylidene-α-D-galactohexodialdo-1,5-pyranose (**17**)*: To a suspension of PDC (4.51 g, 0.012 mol) and NaOAc (1.97 g, 0.024 mol) in anhydrous CH_2Cl_2 (50 mL), was added crushed molecular sieves (4 Å, 4.11 g) at ambient temperature. The suspension was stirred for 1 h. A solution of the compound **16** (1.05 g, 0.04 mol) in anhydrous CH_2Cl_2 (2 mL) was added dropwise, and the reaction was continued for another 6 h at ambient temperature. Hexanes (100 mL) were added, and the mixture was filtered through a thin bed of silica gel using 30% EtOAc−hexanes as the eluent to obtain the desired product **17** as a colorless liquid (854 mg, 0.033 mol, 82% yield). R_f 0.42 (EtOAc : hexanes 2:3). The ^1H and ^{13}C NMR data are consistent with the published data.[27]

*6,7-Dideoxy-1,2:3,4-di-O-isopropylidene-α-D-galacto-hepto-6-enopyranose (**19**)*: To a solution of Ph_3PCH_3Br (2.72 g, 7.63 mmol) in anhydrous THF (15 mL), was added NaH (60% oil dispersion, 254 mg, 7.36 mmol) at ambient temperature. The solution was stirred at 50 °C overnight. A solution of the aldehyde **17** (820 mg, 3.18 mmol) in anhydrous THF (2 mL) was added dropwise to the reaction mixture. After stirring for 2 h, methanol (5 mL) was added to quench the reaction. The reaction mixture was concentrated under reduced pressure, and the obtained crude product was redissolved in EtOAc (80 mL), washed with saturated brine (60 mL × 2), dried over anhydrous Na_2SO_4, filtered, and evaporated. The crude mixture was purified by column chromatography on silica gel using a gradient of 5→15% EtOAc−hexanes as the eluent

to afford the desired alkene **19** as a syrup (615 mg, 2.41 mmol, 74% yield). R_f 0.62 (EtOAc : hexanes 1:4). The ^{1}H and ^{13}C NMR data are consistent with the published data.[27]

*Attempted synthesis of 6-deoxy-1,2:3,4-di-O-isopropylidene-α-D-galacto-heptopyranose (**20**)*: To a solution of the alkene **19** (51 mg, 0.21 mmol) in anhydrous THF (2 mL) was added 1M borane THF complex solution (1.0 mL, 1.0 mmol) dropwise. After the reaction mixture was stirred at ambient temperature for 5 h, a 3M solution of NaOH (1.2 mL, 1.1 mmol) and 50% w/w H_2O_2 solution (0.30 mL, 4.2 mmol) were added. The reaction was continued for another 10 h. TLC (EtOAc : hexanes 1:4) showed the disappearance of the starting material, but several spots were formed. Attempted purification of the mixture by column chromatography did not yield the desired product.

*(Z)- and (E)-7-O-benzyl-6-deoxy-1,2:3,4-di-O-isopropylidene-α-D-galactohepto-6-enopyranose (**23**)*: A solution of Ph_3PCH_2OBnCl (**21**, prepared by heating a solution of benzyl chloromethyl ether (1.0 equiv.) and PPh_3 (1.1 equiv.) in dry toluene at 100 °C for 20 h; 4.68 g, 11.2 mmol) in anhydrous THF (30 mL) was cooled to −78 °C, and a solution of 2.5 M *n*-butyllithium in hexanes (3.7 mL, 9.3 mmol) was added. After stirring for 30 min. a solution of the aldehyde **17** (1.21 g, 4.69 mmol) in anhydrous THF (5 mL) was added dropwise, and the reaction mixture was allowed to warm to ambient temperature overnight. Methanol (5 mL) was added to quench the reaction, and the reaction solution was concentrated under reduced pressure. The crude mixture was redissolved in EtOAc (250 mL), and the solution was washed with saturated brine (80 mL × 2), dried over anhydrous Na_2SO_4, filtered, and evaporated. The crude mixture was purified by column chromatography on silica gel using a gradient of 5→15%

EtOAc−hexanes to afford the desired product **23** as syrup (1.01 g, 2.79 mmol, 60% yield, *Z* : *E* = 1:1). R_f 0.62 (EtOAc : hexanes 1 : 4). Data for *Z*-isomer of **23**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.39-7.29 (m, 5H, Ar), 6.72 (d, 1H, *J* = 12.8 Hz, H-7), 5.56 (d, 1H, *J* = 5.0 Hz, H-1), 5.14 (dd, 1H, *J* = 12.8, 8.8 Hz, H-6), 4.81 (d, 1H, *J* = 11.6 Hz, PhC$\underline{H}_2$), 4.77 (d, 1H, *J* = 11.6 Hz, PhC$\underline{H}_2$), 4.62 (dd, 1H, *J* = 7.8, 2.4 Hz, H-3), 4.30 (dd, 1H, *J* = 5.0, 2.4 Hz, H-2), 4.23 (dd, 1H, *J* = 8.7, 1.9 Hz, H-5), 4.14 (dd, 1H, *J* = 7.9, 1.9 Hz, H-4), 1.54 (s, 3H, Me), 1.50 (s, 3H, Me), 1.36 (s, 3H, Me), 1.35 (s, 3H, Me). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 150.6 (C-7), 128.5 (Ar), 128.0 (Ar), 127.8 (Ar), 109.1 ($\underline{C}(Me)_2$), 108.4 ($\underline{C}(Me)_2$), 99.7 (C-6), 96.6 (C-1), 74.1 (C-4), 71.0 (C-3), 70.9 (Ph$\underline{C}H_2$), 70.3 (C-2), 66.9 (C-5), 26.2 (Me), 26.1 (Me), 24.9 (Me), 24.4 (Me). Data for *E*-isomer of **23**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.39-7.28 (m, 5H, Ar), 6.22 (dd, 1H, *J* = 6.2, 1.0 Hz, H-7), 5.54 (d, 1H, *J* = 4.9 Hz, H-1), 4.94 (ddd, 1H, *J* = 8.5, 1.0, 0.9 Hz, H-5), 4.85 (d, 1H, *J* = 12.6 Hz, PhC$\underline{H}_2$), 4.81 (d, 1H, *J* = 12.6 Hz, PhC$\underline{H}_2$), 4.72 (dd, 1H, *J* = 8.6, 6.2 Hz, H-6), 4.60 (dd, 1H, *J* = 7.9, 2.4 Hz, H-3), 4.29 (dd, 1H, *J* = 5.0, 2.4 Hz, H-2), 4.19 (dd, 1H, *J* = 7.9, 1.9 Hz, H-4), 1.52 (s, 3H, Me), 1.48 (s, 3H, Me), 1.34 (s, 3H, Me), 1.33 (s, 3H, Me). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 147.1 (C-7), 128.5 (Ar), 127.9 (Ar), 127.4 (Ar), 109.1 ($\underline{C}(Me)_2$), 108.6 ($\underline{C}(Me)_2$), 102.8 (C-6), 96.6 (C-1), 74.2 (Ph$\underline{C}H_2$), 73.4 (C-4), 70.9 (C-2), 70.5 (C-3), 62.2 (C-5), 26.1 (Me), 26.0 (Me), 25.2 (Me), 24.4 (Me). HRMS (ESI-QTOF) *m/z*: $[M + H]^+$ calcd for $C_{20}H_{27}O_6$ 363.1808, found 363.1806.

*6-Deoxy-1,2:3,4-di-O-isopropylidene-α-D-galacto-heptopyranose (**20**)*: To a solution of compound **23** (23.3 mg, 0.064 mmol) in methanol (2 mL) was added $Pd(OH)_2$ (20% on charcoal, 10 mg). The solution was stirred under a positive atmosphere of hydrogen gas. After 1 day, the mixture was filtered to remove the catalyst and the solution was evaporated to afford the desired

product **20**[25] as a colorless syrup (13.1 mg, 0.048 mmol, 75% yield). R_f 0.35 (EtOAc : hexanes 2:3). ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 5.55 (d, 1H, J = 5.0 Hz, H-1), 4.63 (dd, 1H, J = 7.9, 2.4 Hz, H-3), 4.34 (dd, 1H, J = 5.1, 2.4 Hz, H-2), 4.17 (dd, 1H, J = 7.9, 1.9 Hz, H-4), 4.03 (ddd, 1H, J = 9.0, 3.8, 3.8 Hz, H-5), 3.87-3.75 (m, 2H, H-7a, H-7b), 2.05 (d, 1H, J = 12.0 Hz, OH-7), 2.00 (dddd, 1H, J = 14.8, 10.0, 6.1, 4.4 Hz, H-6a), 1.87 (dddd, 1H, J = 14.5, 9.3, 5.0, 3.8 Hz, H-6b), 1.56 (s, 3H, Me), 1.49 (s, 3H, Me), 1.37 (s, 3H, Me), 1.36 (s, 3H, Me). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 109.2 ($\underline{C}(Me)_2$), 108.6 ($\underline{C}(Me)_2$), 96.5 (C-1), 73.1 (C-4), 70.9 (C-2), 70.5 (C-3), 65.8 (C-5), 59.9 (C-7), 32.8 (C-6), 26.1 (Me), 26.0 (Me), 24.9 (Me), 24.4 (Me). HRMS (ESI-QTOF) *m/z*: $[M + H]^+$ calcd for $C_{13}H_{23}O_6$ 275.1489, found 275.1492.

*7-O-Benzyl-6-deoxy-1,2:3,4-di-O-isopropylidene-α-D-galacto-heptopyranose (**24**):* To a solution of compound **23** (248 mg, 0.685 mmol) in methanol (3 mL), was added $Pd(OH)_2$ (20% on charcoal, 22 mg). The solution was stirred under a positive atmosphere of hydrogen for 1 h. The catalyst was filtered off and the organic solution was evaporated to afford the desired product **24** as a syrup (238 mg, 0.657 mmol, 96% yield). R_f 0.64 (EtOAc : hexanes 1:4). $[\alpha]_D^{20}$: +45.8° (c 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.37-7.23 (m, 5H, Ar), 5.53 (d, 1H, J = 5.0 Hz, H-1), 4.58 (dd, 1H, J = 7.9, 2.4 Hz, H-3), 4.55 (d, 1H, J = 11.8 Hz, PhC$\underline{H}_2$), 4.49 (d, 1H, J = 11.8 Hz, PhC$\underline{H}_2$), 4.29 (dd, 1H, J = 5.0, 2.4 Hz, H-2), 4.12 (dd, 1H, J = 7.9, 1.8 Hz, H-4), 4.40 (ddd, 1H, J = 9.0, 3.3, 1.8 Hz, H-5), 3.65 (ddd, 1H, J = 9.3, 9.3, 3.7 Hz, H-7a), 3.60 (ddd, 1H, J = 9.6, 9.4, 5.4 Hz, H-7b), 1.97 (dddd, 1H, J = 13.9, 9.5, 5.3, 4.9 Hz, H-6a), 1.90 (dddd, 1H, J = 14.2, 9.8, 5.3, 4.9 Hz, H-6b), 1.52 (s, 3H, Me), 1.48 (s, 3H, Me), 1.36 (s, 3H, Me), 1.35 (s, 3H, Me). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 128.4 (Ar), 127.6 (Ar), 127.4 (Ar), 109.0 ($\underline{C}(Me)_2$), 108.5 ($\underline{C}(Me)_2$), 96.6 (C-1), 73.1 (C-4), 73.0 (Ph$\underline{C}H_2$), 70.9 (C-3), 70.7 (C-2), 66.6 (C-7), 64.1

(C-5), 30.8 (C-6), 26.1 (Me), 26.0 (Me), 25.1 (Me), 24.4 (Me). HRMS (ESI-QTOF) *m/z*: $[M + H]^+$ calcd for $C_{20}H_{29}O_6$ 365.1959, found 365.1966.

*7-O-Benzyl-6-deoxy-1,2,3,4-tetra-O-acetyl-D-galacto-heptopyranose (**25**)*: A solution of compound **24** (1.02 g, 2.82 mmol) in 50% AcOH – H_2O (8 mL) was heated to 80 °C for 8 h. The reaction mixture was evaporated under reduced pressure, and the obtained residue was acetylated using a mixture of Ac_2O (4 mL) and pyridine (4 mL). After stirring for 10 h at ambient temperature, the mixture was evaporated and co-evaporated with toluene three times. The crude mixture was purified by column chromatography on silica gel using 30% EtOAc−hexanes as the eluent to afford the desired product **25** (α/β: 1:1.8) as a syrup (1.185 g, 2.62 mmol, 93% yield). R_f 0.39 (EtOAc : hexanes 2:3). **Data for α anomer**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.42-7.33 (m, 5H, Ar), 6.35 (d, 1H, J = 3.3 Hz, H-1), 5.42 (dd, 1H, J = 3.0, 1.3 Hz, H-4), 5.38-5.33 (m, 2H, H-2 and H-3), 4.37 (dd, 1H, J = 8.9, 4.6 Hz, H-5), 4.55-4.48 (m, 2H, PhC$\underline{H}_2$), 3.59-3.48 (m, 2H, H-7a and H-7b), 2.17 (s, 3H, Ac), 2.09 (s, 3H, Ac), 2.04 (s, 3H, Ac), 2.02 (s, 3H, Ac), 1.98-1.86 (m, 1H, H-6a), 1.85-1.69 (m, 1H, H-6b). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 128.4 (Ar), 127.7 (Ar), 127.6 (Ar), 89.8 (C-1), 73.1 (Ph$\underline{C}H_2$), 69.9 (C-3), 67.9 (C-4), 67.8 (C-5), 66.7 (C-2), 65.4 (C-7), 30.7 (C-6), 20.8 (Ac), 20.7 (Ac), 20.6 (Ac), 20.5 (Ac). **Data for β anomer**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.42-7.27 (m, 5H, Ar), 5.70 (d, 1H, J = 7.9 Hz, H-1), 5.38-5.32 (m, 2H, H-2 and H-4), 5.11 (dd, 1H, J = 10.4, 3.4 Hz, H-3), 4.48-4.43 (m, 2H, PhC$\underline{H}_2$), 4.04 (ddd, 1H, J = 8.5, 4.8, 1.1 Hz, H-5), 3.59-3.48 (m, 2H, H-7a and H-7b), 2.18 (s, 3H, Ac), 2.13 (s, 3H, Ac), 2.06 (s, 3H, Ac), 2.01 (s, 3H, Ac), 1.98-1.86 (m, 1H, H-6a), 1.85-1.69 (m, 1H, H-6b). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 128.4 (Ar), 127.7 (Ar), 127.5 (Ar), 92.4 (C-1), 73.2 (Ph$\underline{C}H_2$), 71.3 (C-5),

71.2 (C-3), 69.3 (C-2), 68.2 (C-4), 66.5 (C-7), 30.8 (C-6), 20.8 (Ac), 20.7 (Ac), 20.7 (Ac), 20.5 (Ac). HRMS (ESI-QTOF) *m/z*: $[M + NH_4]^+$ calcd for $C_{22}H_{32}NO_{10}$ 470.2021, found 470.2016.

*7-O-Benzyl-6-deoxy-2,3,4-tri-O-acetyl-D-galacto-heptopyranose (**26**)*: To a solution of compound **25** (560 mg, 1.24 mmol) in anhydrous DMF (4 mL), was added hydrazinium acetate (126 mg, 1.36 mmol), and the mixture was stirred at ambient temperature for 4 h. The mixture was diluted with EtOAc (80 mL), extracted with brine (50 mL × 2), dried over anhydrous Na_2SO_4, and evaporated. The crude product was purified by column chromatography on silica gel using 40% EtOAc−hexanes as the eluent to afford the pure product **26** (α/β: 1:2.3) as a syrup (434 mg, 1.06 mmol, 85% yield). R_f 0.34 (EtOAc : hexanes 2:3). **Data for α anomer**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.38-7.25 (m, 5H, Ar), 5.28 (dd, 1H, J = 2.7, 1.2 Hz, H-4), 5.08-5.01 (m, 2H, H-2 and H-3), 4.60 (broad, 1H, H-1), 4.53-4.46 (m, 2H, PhC$\underline{H}_2$), 3.91 (ddd, 1H, J = 8.7, 4.7, 1.1 Hz, H-5), 3.60-3.44 (m, 2H, H-7a, H-7b), 2.14 (s, 3H, Ac), 2.09 (s, 3H, Ac), 1.99 (s, 3H, Ac), 1.93-1.81 (m, 1H, H-6a), 1.80-1.66 (m, 1H, H-6b). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 127.8 (Ar), 127.7 (Ar), 127.6 (Ar), 95.8 (C-1), 73.0 (Ph$\underline{C}H_2$), 71.4 (C-3), 70.8 (C-4), 70.2 (C-5), 69.6 (C-2), 65.4 (C-7), 30.8 (C-6), 20.7 (Ac), 20.6 (Ac), 20.5 (Ac). **Data for β anomer**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.38-7.27 (m, 5H, Ar), 5.43-5.38 (m, 2H, H-1 and H-2), 5.34 (dd, 1H, J = 3.4, 1.3 Hz, H-4), 5.13 (dd, 1H, J = 10.8, 3.6 Hz, H-3), 4.45-4.36 (m, 2H, PhC$\underline{H}_2$), 4.41 (ddd, 1H, J = 8.3, 5.0, 1.4 Hz, H-5), 3.58-3.47 (m, 2H, H-7a and H-7b), 2.13 (s, 3H, Ac), 2.08 (s, 3H, Ac), 1.98 (s, 3H, Ac), 1.93-1.81 (m, 1H, H-6a), 1.80-1.66 (m, 1H, H-6b). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 128.4 (Ar), 127.8 (Ar), 127.6 (Ar), 90.5 (C-1), 72.8 (Ph$\underline{C}H_2$), 70.5 (C-4), 68.5 (C-3), 67.7 (C-2), 65.5 (C-7), 65.2 (C-5), 30.6 (C-6), 20.8 (Ac), 20.7 (Ac), 20.6 (Ac). HRMS (ESI-QTOF) *m/z*: $[M + NH_4]^+$ calcd for $C_{20}H_{30}NO_9$ 428.1915, found 428.1924.

*7-O-Benzyl-6-deoxy-2,3,4-tri-O-acetyl-D-galacto-heptopyranosyl trichloroacetimidate (**27**)*: To a solution of compound **26** (362 mg, 0.88 mmol) in anhydrous CH_2Cl_2 (5 mL) was added K_2CO_3 (244 mg, 1.76 mmol) and trichloroacetonitrile (0.5 mL, 4.5 mmol), and the reaction mixture was stirred at ambient temperature for 12 h. The solution was evaporated under reduced pressure. The crude product was dissolved in EtOAc (50 mL), extracted with brine (30 mL × 2) and the organic layer was evaporated and co-evaporated with toluene to afford the crude product **27** (α/β: 1:1) as a colorless syrup. R_f 0.42 (EtOAc : hexanes 2:3). The crude product was used directly for next step without further purification.

*6-Azidohexyl 3,4-di-O-acetyl-7-O-benzyl-6-deoxy-β-D-galacto-heptopyranoside (**30**) and 6-Azidohexyl 2,3,4-tri-O-acetyl-7-O-benzyl-6-deoxy-β-D-galacto-heptopyranoside (**29**)*: A mixture of imidate **27** (136 mg, 0.247 mmol), alcohol **28** (177 mg, 1.24 mmol) and molecular sieves (4 Å, crushed, 500 mg) in anhydrous CH_2Cl_2 (5 mL) was stirred for 1 h at ambient temperature under an atmosphere of argon. The mixture was then cooled down to -40 °C and TMSOTf (50 μL) was added dropwise. After stirring for 4 h, the temperature was gradually warmed up to ambient temperature. A few drops of triethylamine were added to quench the reaction, and the mixture was filtered off through a thin bed of celite, and washed with EtOAc (~40 mL). The organic solution was washed with brine (20 mL), dried over Na_2SO_4, and evaporated. The crude mixture was purified by column chromatography on silica gel using 20% EtOAc−hexane as the eluent to afford the pure product **30** as a syrup (90.2 mg, 0.182 mmol, 77% yield). When a similar reaction of imidate **27** (245 mg, 0.442 mmol) and alcohol **28** (95.1 mg, 0.665 mmol) was carried, compound **29** (93.2 mg, 0.189 mmol, 43% yield) and the 2-*O*-deacetylated product **30**

(59.8 mg, 0.112 mmol, 25% yield) were obtained. Data for compound **30:** R_f 0.37 (EtOAc : hexanes 3:7). $[\alpha]_D^{20}$: +57.1° (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.41-7.29 (m, 5H, Ar), 5.30 (dd, 1H, *J* = 3.5, 1.1 Hz, H-4), 4.96 (dd, 1H, *J* = 10.2, 3.5 Hz, H-3), 4.56 (d, 1H, *J* = 11.9 Hz, PhC$\underline{H}_2$), 4.46 (d, 1H, *J* = 11.9 Hz, PhC$\underline{H}_2$), 4.29 (d, 1H, *J* = 7.7 Hz, H-1), 3.89 (dd, 1H, *J* = 8.7, 4.1 Hz, H-5), 3.85 (ddd, 1H, *J* = 13.3, 6.6, 6.6 Hz, OC$\underline{H}_a$H$_b$), 3.78 (dd, 1H, *J* = 10.2, 7.7 Hz, H-2), 3.64-3.56 (m, 1H, H-7a), 3.55-3.49 (m, 1H, H-7b), 3.49 (ddd, 1H, *J* = 13.8, 6.8, 6.8 Hz, OCH$_a\underline{H}_b$), 3.29 (t, 2H, *J* = 6.8 Hz, -CH_2N_3), 2.31 (broad, 1H, 2-OH), 2.14 (s, 3H, Ac), 2.07, (s, 3H, Ac), 1.91 (dddd, 1H, *J* = 13.9, 9.5, 5.3, 4.9 Hz, H-6a), 1.78 (dddd, 1H, *J* = 14.0, 9.8, 4.9, 4.9 Hz, H-6b), 1.70-1.56 (m, 4H, 2 × CH_2), 1.48-1.35 (m, 4H, 2 × CH_2). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 170.4 (Ac), 170.3 (Ac), 128.4 (Ar), 127.8 (Ar), 127.7 (Ar), 103.1 (C-1), 73.1 (Ph$\underline{C}H_2$), 73.0 (C-3), 70.0 (CH_2), 69.9 (C-5), 69.7 (C-4), 69.4 (C-2), 65.6 (C-7), 51.3 (CH_2), 30.9 (C-6), 29.4 (CH_2), 28.7 (CH_2), 26.4 (CH_2), 25.4 (CH_2), 20.8 (Ac), 20.7 (Ac). HRMS (ESI-QTOF) *m/z*: $[M + NH_4]^+$ calcd for $C_{24}H_{39}N_4O_8$ 511.2762, found 511.2762. Data for compound **29**: R_f 0.55 (EtOAc : hexanes 3:7). $[\alpha]_D^{20}$: +32.3° (c 0.99, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.38-7.28 (m, 5H, Ar), 5.28 (dd, 1H, *J* = 3.5, 1.1 Hz, H-4), 5.16 (dd, 1H, *J* = 10.4, 7.9 Hz, H-2), 5.02 (dd, 1H, *J* = 10.4, 3.4 Hz, H-3), 4.53 (d, 1H, *J* = 12.0 Hz, PhC$\underline{H}_2$), 4.44 (d, 1H, *J* = 12.0 Hz, PhC$\underline{H}_2$), 4.38 (d, 1H, *J* = 7.9 Hz, H-1), 3.87 (ddd, 1H, *J* = 8.7, 4.6, 1.3 Hz, H-5), 3.79 (ddd, 1H, *J* = 9.6, 6.2, 6.2 Hz, OC$\underline{H}_a$H$_b$), 3.61-3.55 (m, 1H, H-7a), 3.50 (ddd, 1H, *J* = 9.4, 5.2, 5.2 Hz, H-7b), 3.38 (ddd, 1H, *J* = 9.6, 7.2, 6.3 Hz, OCH$_a\underline{H}_b$), 3.25 (t, 2H, *J* = 6.9 Hz, -CH_2N_3), 2.14 (s, 3H, Ac), 2.07, (s, 3H, Ac), 1.98, (s, 3H, Ac), 1.89-1.80 (m, 1H, H-6a), 1.78-1.69 (m, 1H, H-6b), 1.63-1.51 (m, 4H, 2 × CH_2), 1.42-1.32 (m, 4H, 2 × CH_2). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 170.5 (Ac), 170.1 (Ac), 169.4 (Ac), 129.5 (Ar), 128.4 (Ar), 127.7 (Ar), 101.2 (C-1), 73.1 (Ph$\underline{C}H_2$), 71.3 (C-3), 69.8 (C-4), 69.7 (CH_2), 69.6 (C-2), 69.2 (C-5), 65.5 (C-7), 51.3 (CH_2), 30.8 (C-6), 29.3

(CH_2), 28.7 (CH_2), 26.4 (CH_2), 25.4 (CH_2), 20.8 (Ac), 20.7 (Ac), 20.6 (Ac). HRMS (ESI-QTOF) *m/z*: $[M + NH_4]^+$ calcd for $C_{26}H_{41}N_4O_9$ 553.2868, found 553.2882.

*6-Azidohexyl 3,4-di-O-acetyl-7-O-benzyl-6-deoxy-2-O-mesyl-β-D-galacto-heptopyranoside (**31**)*: Compound **30** (57.2 mg, 0.116 mmol) was dissolved in anhydrous pyridine (1.0 mL) and methanesulfonyl chloride (20 μL, 0.232 mmol) was added. The mixture was stirred at ambient temperature for 6 h. Methanol (0.5 mL) was added to quench the reaction, and the crude mixture was evaporated and co-evaporated with toluene to dry. The residue was redissolved in EtOAc (~30 mL), and the organic solution was successively washed with aqueous HCl (1 M, 10 mL), aqueous NaOH (1 M, 10 mL) and saturated brine (20 mL), dried over Na_2SO_4, and evaporated. The crude material was purified by column chromatography on silica gel using a gradient of 25→30% EtOAc- hexanes as the eluent to afford the pure product **31** as a syrup (60.4 mg, 0.106 mmol, 91% yield). R_f 0.44 (EtOAc : hexanes 3:7). $[\alpha]_D^{20}$: +37.9° (c 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.39-7.26 (m, 5H, Ar), 5.31 (dd, 1H, *J* = 3.5, 0.8 Hz, H-4), 5.08 (dd, 1H, *J* = 10.2, 3.5 Hz, H-3), 4.66 (dd, 1H, *J* = 10.2, 7.9 Hz, H-2), 4.53 (d, 1H, *J* = 11.9 Hz, PhC$\underline{H}_2$), 4.44 (d, 1H, *J* = 7.9 Hz, H-1), 4.47 (d, 1H, *J* = 11.9 Hz, PhC$\underline{H}_2$), 3.88 (dd, 1H, *J* = 8.7, 4.2 Hz, H-5), 3.80 (ddd, 1H, *J* =13.5, 6.8, 6.8 Hz, OC$\underline{H}_a$H$_b$), 3.56 (ddd, 1H, *J* = 9.0, 8.7, 4.4 Hz, H-7a), 3.49 (ddd, 1H, *J* = 9.9, 5.0, 5.0 Hz, H-7b), 3.46 (ddd, 1H, *J* = 13.4, 6.7, 6.7 Hz, OCH$_a\underline{H}_b$), 3.26 (t, 2H, *J* = 6.8 Hz, -CH_2N_3), 3.05 (s, 3H, Ms), 2.14 (s, 3H, Ac), 2.05 (s, 3H, Ac), 1.87 (dddd, 1H, *J* = 13.9, 9.5, 5.3, 4.5 Hz, H-6a), 1.76 (dddd, 1H, *J* = 14.0, 9.8, 5.2, 5.2 Hz, H-6b), 1.66-1.55 (m, 4H, 2 × CH_2), 1.44-1.32 (m, 4H, 2 × CH_2). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 170.3 (Ac), 169.8 (Ac), 128.4 (Ar), 127.8 (Ar), 127.7 (Ar), 100.4 (C-1), 77.5 (C-2), 73.1 (Ph$\underline{C}H_2$), 70.7 (C-5), 70.0 (C-4), 69.9 (CH_2), 69.8 (C-3), 66.4 (C-7), 51.3 (CH_2), 39.0 (Ms), 30.7 (C-6), 29.4 (CH_2), 28.7

(CH_2), 26.4 (CH_2), 25.4 (CH_2), 20.6 (Ac), 20.5 (Ac). HRMS (ESI-QTOF) *m/z*: $[M + NH_4]^+$ calcd for $C_{25}H_{41}N_4O_{10}S$ 589.2538, found 589.2532.

*6-Azidohexyl 7-O-benzyl-6-deoxy-2-O-mesyl-β-D-galacto-heptopyranoside (**32**)*: To a solution of compound **31** (33.5 mg, 0.058 mmol) in benzyl alcohol (1.0 mL) was added KOBu-*t* (20 mg) at ambient temperature, and the reaction mixture was stirred for 1 h until TLC showed the disappearance of the starting material. The reaction mixture was diluted with EtOAc (30 mL) and the organic solution was washed with brine (20 mL), dried over anhydrous Na_2SO_4 and evaporated. The crude mixture was then purified by column chromatography on silica gel using 50% EtOAc-hexanes to afford the pure compound **32** as a syrup (21.1 mg, 0.044 mmol, 75% yield). R_f 0.26 (EtOAc : hexanes 1:1). $[\alpha]_D^{20}$: +47.3° (c 0.98, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.39-7.26 (m, 5H, Ar), 4.54 (d, 1H, J = 11.9 Hz, PhC$\underline{H}_2$), 4.47 (d, 1H, J = 11.9 Hz, PhC$\underline{H}_2$), 4.45 (dd, 1H, J = 9.4, 7.9 Hz, H-2), 4.34 (d, 1H, J = 7.9 Hz, H-1), 3.83 (dd, 1H, J = 5.2, 3.4 Hz, H-4), 3.81-3.76 (m, 1H, OC$\underline{H}_aH_b$), 3.73 (dd, 1H, J = 9.4, 3.5 Hz, H-3), 3.66 (dd, 1H, J = 7.2, 5.9 Hz, H-5), 3.63-3.55 (m, 2H, H-7a, H-7b), 3.45 (ddd, 1H, J = 9.5, 6.7, 6.7 Hz, OC$H_a\underline{H}_b$), 3.25 (t, 2H, J = 6.8 Hz, -CH_2N_3), 3.12 (s, 3H, Ms), 2.06 (dddd, 1H, J = 13.2, 7.7, 5.3, 3.9 Hz, H-6a), 1.96 (dddd, 1H, J = 14.7, 8.0, 5.2, 5.2 Hz, H-6b), 1.66-1.52 (m, 4H, 2 × CH_2), 1.43-1.32 (m, 4H, 2 × CH_2). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 128.4 (Ar), 127.8 (Ar), 127.7 (Ar), 100.0 (C-1), 81.8 (C-2), 73.2 (Ph$\underline{C}H_2$), 72.1 (C-3), 71.4 (C-5), 70.7 (C-4), 69.6 (CH_2), 65.8 (C-7), 51.3 (CH_2), 38.5 (Ms), 30.7 (C-6), 29.4 (CH_2), 28.7 (CH_2), 26.4 (CH_2), 25.4 (CH_2). HRMS (ESI-QTOF) *m/z*: $[M + NH_4]^+$ calcd for $C_{21}H_{37}N_4O_8S$ 505.2327, found 505.2326.

*6-Azidohexyl 2,3-anhydro-7-O-benzyl-6-deoxy-β-D-talo-heptopyranoside (**33**)*: To a solution of the compound **32** (72 mg, 0.143 mmol) in benzyl alcohol (1.0 mL) was added KOBu-*t* (52 mg, 0.377 mmol), and the reaction was continued at ambient temperature for 12 h. The reaction mixture was diluted with EtOAc (30 mL) and washed with brine (20 mL × 2). The organic layer was dried over anhydrous Na_2SO_4, and evaporated. The crude mixture was then purified by column chromatography on silica gel using a gradient of 7→15% EtOAc-CH_2Cl_2 as the eluent to afford the pure product **33** as a syrup (49.7 mg, 0.123 mmol, 86% yield). R_f 0.42 (EtOAc : hexanes 1:1). $[\alpha]_D^{20}$: +30.5° (c 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.38-7.26 (m, 5H, Ar), 4.70 (d, 1H, *J* = 0.2 Hz, H-1), 4.54 (d, 1H, *J* = 12.1 Hz, PhC$\underline{H}_2$), 4.45 (d, 1H, *J* = 12.1 Hz, PhC$\underline{H}_2$), 3.87 (ddd, 1H, *J* = 13.0, 6.5, 6.5 Hz, OC$\underline{H}_a$H$_b$), 3.72 (broad, 1H, H-4), 3.66-3.55 (m, 2H, H-7a and H-7b), 3.57 (t, 1H, *J* = 0.9 Hz, H-3), 3.53 (dd, 1H, *J* = 5.4, 2.7 Hz, H-5), 3.47 (ddd, 1H, *J* = 13.6, 6.8, 6.8 Hz, OCH$_a\underline{H}_b$), 3.30 (d, 1H, *J* = 3.8 Hz, H-2), 3.29 (t, 2H, *J* = 6.8 Hz, -CH_2N_3), 2.43 (d, 1H, *J* = 11.7 Hz, OH-4), 1.97 (dddd, 1H, *J* = 18.0, 13.9, 9.5, 5.5 Hz, H-6a), 1.91 (dddd, 1H, *J* = 18.5, 12.9, 9.3, 5.5 Hz, H-6b), 1.73-1.55 (m, 4H, 2 × CH_2), 1.49-1.36 (m, 4H, 2 × CH_2). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 128.4 (Ar), 127.7 (Ar), 127.6 (Ar), 97.4 (C-1), 74.2 (C-5), 73.0 (Ph$\underline{C}H_2$), 69.6 (CH_2), 66.0 (C-7), 62.9 (C-4), 71.2 (C-5), 54.2 (C-3), 52.9 (C-2), 51.4 (CH_2), 31.0 (C-6), 29.7 (CH_2), 29.5 (CH_2), 26.5 (CH_2), 25.6 (CH_2). HRMS (ESI-QTOF) *m/z*: $[M + NH_4]^+$ calcd for $C_{20}H_{33}N_4O_5$ 409.2445, found 409.2433.

*6-Azidohexyl 3,7-di-O-benzyl-6-deoxy-β-D-ido-heptopyranoside (**34**)*: To the solution of the compound **33** (35 mg, 0.089 mmol) in benzyl alcohol (1 mL) was added KOBu-*t* (30 mg, 0.22 mmol). The reaction mixture was stirred for 12 h at 60 °C. The reaction mixture was diluted with EtOAc (30 mL) and washed with saturated brine (20 mL). The organic layer was dried over

anhydrous Na_2SO_4, filtered, and evaporated. The crude material was then purified by column chromatography on silica gel using a gradient of 7→10% EtOAc-CH_2Cl_2 as the eluent to afford the pure product **34** as a syrup (29.6 mg, 0.059 mmol, 67% yield). Compound **34** could also be synthesized from compound **31** in 63% yield by reaction with KOBu-*t* in benzyl alcohol by gradually raising the temperature to 60 °C. R_f 0.45 (EtOAc : hexanes1:1). $[\alpha]_D^{20}$: -52.5° (c 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.38-7.25 (m, 10H, Ar), 4.68 (d, 1H, J = 0.7 Hz, H-1), 4.63 (d, 1H, J = 11.8 Hz, PhC$\underline{H}_2$), 4.58 (d, 1H, J = 11.8 Hz, PhC$\underline{H}_2$), 4.55 (d, 1H, J = 11.9 Hz, PhC$\underline{H}_2$), 4.49 (d, 1H, J = 11.9 Hz, PhC$\underline{H}_2$), 4.03 (dd, 1H, J = 8.5, 5.2 Hz, H-5), 3.91 (t, 1H, J = 2.6 Hz, H-3), 3.86 (ddd, 1H, J = 9.6, 6.6, 6.6 Hz, OC$\underline{H}_a$H$_b$), 3.78 (broad, 1H, H-2), 3.69-3.63 (m, 2H, H-7a and H-7b), 3.58-3.46 (m, 3H, H-4, OCH$_a\underline{H}_b$, OH-4), 3.26 (t, 2H, J = 6.8 Hz, -CH_2N_3), 2.74 (broad, 1H, OH-2), 2.12 (dddd, 1H, J = 18.0, 13.9, 9.5, 5.5 Hz, H-6a), 1.98 (dddd, 1H, J = 18.5, 12.9, 9.3, 5.5 Hz, H-6b), 1.66-1.56 (m, 4H, 2 × CH_2), 1.44-1.32 (m, 4H, 2 × CH_2). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 128.5 (Ar), 128.4 (Ar), 127.9 (Ar), 127.7 (Ar), 127.6 (Ar), 127.5 (Ar), 98.4 (C-1), 76.4 (C-3), 73.0 (Ph$\underline{C}$H$_2$), 72.3 (Ph$\underline{C}$H$_2$), 71.2 (C-5), 69.1 (CH_2), 68.9 (C-2), 68.0 (C-4), 66.3 (C-7), 51.4 (CH_2), 31.0 (C-6), 29.7 (CH_2), 29.4 (CH_2), 26.5 (CH_2), 25.6 (CH_2). HRMS (ESI-QTOF) *m/z*: $[M + Na]^+$ calcd for $C_{27}H_{37}N_3O_6Na$ 522.2575, found 522.2567.

*6-Azidohexyl 3-O-allyl-7-O-benzyl-6-deoxy-β-D-ido-heptopyranoside (**35**)*: To the solution of the compound **33** (156 mg, 0.397 mmol) in allyl alcohol (1.5 mL) was added KOBu-*t* (101 mg, 0.901 mmol). The reaction mixture was stirred for 12 h at 60 °C until TLC showed the disappearance of the starting material. The reaction mixture was diluted with EtOAc (30 mL) and washed with brine (20 mL × 2). The organic layer was dried over anhydrous Na_2SO_4, filtered, and evaporated. The crude material was then purified by column chromatography on

silica gel using a gradient of 5→10% EtOAc-CH_2Cl_2 as the eluent to afford the pure product **35** as a syrup (129.7 mg, 0.289 mmol, 73% yield). R_f 0.46 (EtOAc : hexanes 1:1). $[\alpha]_D^{20}$: -62.1° (c 1.01, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.39-7.25 (m, 5H, Ar), 5.87 (dddd, 1H, *J* = 21.7, 15.9, 10.5, 5.5 Hz, -OCH_2-C<u>H</u>=CH_2), 5.28 (ddd, 1H, *J* = 17.1, 3.2, 1.6 Hz, -OCH_2-CH=C<u>H</u>$_2$), 5.20 (ddd, 1H, *J* = 10.3, 2.7, 1.5 Hz, -OCH_2-CH=C<u>H</u>$_2$), 4.64 (d, 1H, *J* = 1.1 Hz, H-1), 4.55 (d, 1H, *J* = 12.1 Hz, PhC<u>H</u>$_2$), 4.49 (d, 1H, *J* = 12.1 Hz, PhC<u>H</u>$_2$), 4.08 (dddd, 1H, *J* = 15.5, 5.6, 1.5, 1.5 Hz -OC<u>H</u>$_2$-CH=CH_2), 4.04 (dddd, 1H, *J* = 15.7, 5.5, 1.4, 1.4 Hz -OC<u>H</u>$_2$-CH=CH_2), 3.98 (dd, 1H, *J* = 8.5, 5.1 Hz, H-5), 3.85 (dd, 1H, *J* = 12.9, 6.6 Hz, OC<u>H</u>$_a$H$_b$), 3.82 (dd, 1H, *J* = 2.1, 1.7 Hz, H-3), 3.77 (broad, 1H, H-2), 3.67-3.60 (m, 2H, H-7a and H-7b), 3.51-3.43 (m, 3H, H-4, OCH_a<u>H</u>$_b$, OH-4), 3.26 (t, 2H, *J* = 6.9 Hz, -CH_2N_3), 2.77 (d, 1H, *J* = 2.0 Hz, OH-2), 2.09 (dddd, 1H, *J* = 18.0, 13.9, 9.5, 5.5 Hz, H-6a), 1.94 (dddd, 1H, *J* = 18.5, 12.9, 9.3, 5.5 Hz, H-6b), 1.66-1.56 (m, 4H, 2 × CH_2), 1.38-1.32 (m, 4H, 2 × CH_2). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 134.2 (-OCH_2-<u>C</u>H=CH_2), 128.4 (Ar), 127.6 (Ar), 127.5 (Ar), 117.4 (-OCH_2-CH=<u>C</u>H_2), 98.4 (C-1), 76.1 (C-3), 73.0 (Ph<u>C</u>H_2), 71.2 (-O<u>C</u>H_2-CH=CH_2), 71.1 (C-5), 69.1 (CH_2), 68.9 (C-2), 68.0 (C-4), 66.3 (C-7), 51.3 (CH_2), 31.0 (C-6), 29.4 (CH_2), 28.7 (CH_2), 26.4 (CH_2), 25.6 (CH_2). HRMS (ESI-QTOF) *m/z*: $[M + Na]^+$ calcd for $C_{23}H_{35}N_3O_6Na$ 472.2418, found 472.2400.

*6-Aminohexyl 6-deoxy-β-D-ido-heptopyranoside acetic acid salt (**2**)*: To the solution of the compound **34** (11 mg, 22 μmol) in methanol/CH_2Cl_2 (2 mL/0.5 mL) was added palladium hydroxide (20% $Pd(OH)_2$ on charcoal; 15 mg), acetic acid (2 drops) and water (5 drops). The solution was stirred under positive pressure hydrogen gas for 2 days. The mixture was filtered and evaporated to afford the product **2** as a colorless syrup (6.2 mg, 21 μmol, 96% yield). R_f 0.21 (MeOH : CH_2Cl_2 3:7). HRMS (ESI-QTOF, **2**) m/z: $[M + H]^+$ calcd for $C_{13}H_{28}NO_6$

294.1911, found 294.1908. The ^{1}H NMR experiment showed the presence of partially *N*-methylated side products. HRMS (ESI-QTOF, mono-N-methylated) *m/z*: $[M + H]^+$ calcd for $C_{14}H_{30}NO_6$ 308.2073, found 308.1995. HRMS (ESI-QTOF, N,N-dimethylated) *m/z*: $[M + H]^+$ calcd for $C_{15}H_{32}NO_6$ 322.2230, found 322.2155. Birch reduction: Liquid NH_3 (~20 mL) was collected in a flask with the help of a dry-ice condenser to -78 °C. Sodium metal (~44 mg) was added, and the solution turn dark blue. A solution of the compound **34** (16 mg, 32 μmol) in THF (1 mL) was added dropwise, and the solution was stirred at -78 °C for 1 h. MeOH (0.5 mL) was added to quench the reaction, and the solution was allowed to warm up to ambient temperature. After the evaporation of ammonia, the mixture was redissolved in MeOH (~5 mL) and neutralized with AcOH. The solution was evaporated to dryness and the residue was subjected to a gel filtration on Sephadex LH-20 using MeOH as the eluent to afford the pure product **2** which was further purified by reverse-phase chromatography on Sep-Pak (C18) using 0→20% MeOH-H_2O (containing 0.2% AcOH) as the eluent. Compound **2** was obtained as syrup (8.9 mg, 31 μmol, 95% yield). $[\alpha]_D^{20}$: -9.7° (c 0.37, MeOH). ^{1}H NMR (D_2O, 400 MHz): δ_H 4.72 (s, 1H, H-1), 3.97 (t, 1H, J = 3.6 Hz, H-3), 3.94 (dd, 1H, J = 3.9, 1.8 Hz, H-4), 3.79 (ddd, 1H, J = 9.9, 6.8, 6.8 Hz, $OC\underline{H}_aH_b$), 3.69-3.64 (m, 2H, H-7a and H-7b), 3.61 (d, J = 2.6 Hz, H-2), 3.60-3.54 (m, 1H, $OCH_a\underline{H}_b$), 3.43 (dd, 1H, J = 1.7, 1.7 Hz, H-5), 2.88 (t, 2H, J = 7.4 Hz, $-CH_2N_3$), 1.91 (dddd, 1H, J = 14.9, 10.3, 5.3, 5.3 Hz, H-6a), 1.70 (dddd, 1H, J = 14.8, 7.5, 7.5, 3.9 Hz, H-6b), 1.60-1.47 (m, 4H, 2 × CH_2), 1.36-1.25 (m, 4H, 2 × CH_2). ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 98.9 (C-1), 71.1 (C-5), 69.8 (C-3, C-4), 69.7 (OCH_aH_b), 69.4 (C-2), 58.1 (C-7), 39.4 (CH_2NH_2), 32.4 (C-6), 28.5 (CH_2), 26.7 (CH_2), 25.3 (CH_2), 24.6 (CH_2). HRMS (ESI-QTOF) *m/z*: $[M + H]^+$ calcd for $C_{13}H_{28}NO_6$ 294.1911, found 294.1908.

Supporting Information

^{1}H, ^{13}C, ^{1}H-^{1}H gCOSY and ^{1}H-^{13}C gHSQC NMR spectra are provided for all synthesized compounds.

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