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New and general synthesis of β-*C*-glycosylformaldehydes from easily available β-*C*-glycosylpropanones

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Abstract—A highly effective method for the introduction of a formyl group at the anomeric position of pyranosides was developed via enolisation of β-*C*-D-glycopyranosylpropan-2-one using thermodynamic conditions then oxidative cleavage of the more substituted double bond. This sequence affords the desired aldehydes that are conveniently protected as aminals for purification and storage and easily regenerated using Dowex resin H^+. In this paper, the syntheses of nine differently protected aldehydes derived from D-glucose, D-galactose, lactose and *N*-acetyl-D-glucosamine are presented. Our strategy proved to be very efficient in most cases excepted in the D-mannose series.

Keywords: *C*-Glycosyl compounds; Sugar aldehydes; Enoxysilanes; α-Hydroxyketones; Aminals

1. Introduction

C-Glycosyl compounds, in which the anomeric oxygen atom is replaced by a methylene group, have been the subject of considerable interest in carbohydrate chemistry.[1,2] These carbohydrate mimetics possess an improved stability towards acid-, base and enzymatic hydrolysis and may display interesting biological activities.[1c,d,2g,3] They may serve as regulators of enzymes such as glycosidases and glycosyltransferases that are potential anti-cancer, antiviral or antidiabetic agents. They may also be used as artificial ligands that can be useful in probing cellular interactions. Moreover, despite structural investigations that revealed, most of the time, notable conformational differences between the natural and unnatural glycosides,[4] a number of studies have shown that the biological properties of *C*-glycosyl compounds are retained and sometimes even greater.[3a,d–g,k,n–r] Consequently, a number of reliable methods have been developed for the synthesis of these compounds. One way for achieving the preparation of complex *C*-glycosyl compounds is the coupling between *C*-glycosylformaldehydes and another sugar moiety or an aglycone residue. This method was already proved to be very useful for the preparation of *C*-linked glycopeptides, *C*-linked glycolipids and *C*-linked disaccharides.[3d,5] Peracetylated glycopyranosylformaldehydes can be synthesised by reductive hydrolysis of pyranosylcyanide or by ozonolyzis of nitro sugar-derived silyl nitronates.[6] Perbenzylated glycopyranosylformaldehydes can be synthesised by ozonolyzis of *C*-glycosylallenes[7] or, in most cases, from 2,3,4,6-tetra-*O*-benzyl-D-glycono-1,5-lactone after anomeric introduction of phenylacetylene,[8] dithiane,[8,9] thiazole or benzothiazole ring[10] from which the formyl group can be generated. However, several drawbacks appear to be associated with some of these methodologies such as moderate overall yields or the presence of an α/β anomeric mixture thus limiting their use. We describe here an efficient alternative protocol for incorporating a formyl

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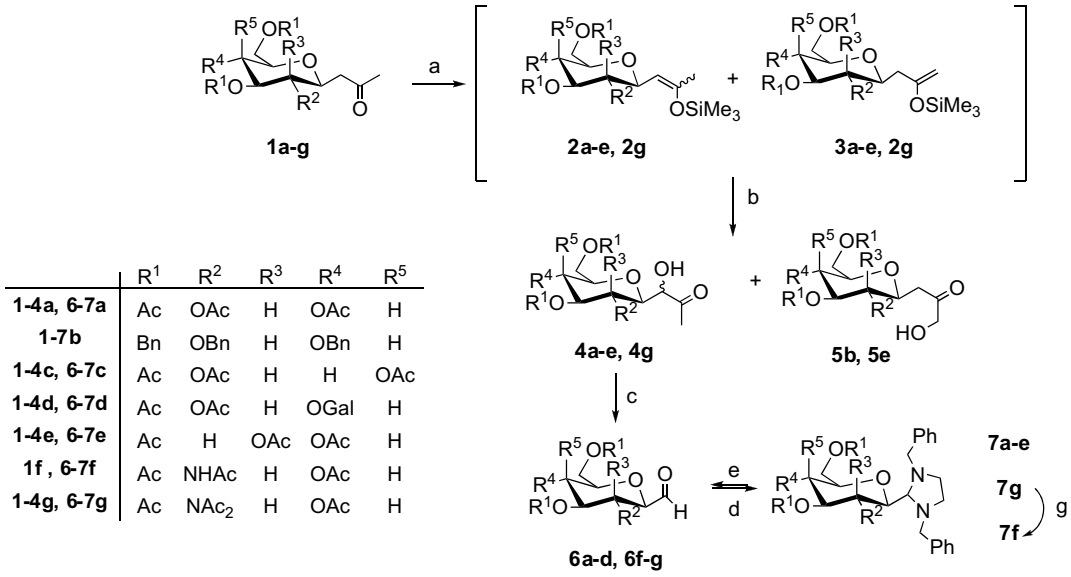


	R^1	R^2	R^3	R^4	R^5
1-4a, 6-7a	Ac	OAc	H	OAc	H
1-7b	Bn	OBn	H	OBn	H
1-4c, 6-7c	Ac	OAc	H	H	OAc
1-4d, 6-7d	Ac	OAc	H	OGal	H
1-4e, 6-7e	Ac	H	OAc	OAc	H
1f , 6-7f	Ac	NHAc	H	OAc	H
1-4g, 6-7g	Ac	NAc_2	H	OAc	H

Scheme 1. Reagents and conditions: (a) see conditions of Table 1; (b) dimethyldioxirane; (c) $NaIO_4$, THF–water; (d) *N*,*N*-dibenzylethylenediamine, toluene; (e) Dowex H^+ resin, water–THF; (f) isopropenylacetate, TsOH (**1g**, 99%); (g) NH_2–NH_2, water, CH_2Cl_2 (**7f**, 88%).

group at the anomeric position of a sugar derivative, which may serve as a general tool towards the synthesis of more complex *C*-glycosyl compounds or *C*-disaccharides of biological relevance.

Our approach towards the synthesis of sugar aldehydes is described in Scheme 1. It is based on the use of peracetylated β-*C*-glycosylketones **1** for which a very easy two-step synthesis was recently described.[11,12] In this strategy, we postulated that enolisation of ketones **1** in thermodynamic conditions followed by oxidative cleavage of the more substituted double bond would furnish the desired aldehydes **6**.

2. Results and discussion

We started our study with the preparation of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylformaldehyde **6a**.[13] The enolisation of **1a**[12] was performed under various conditions and the results are presented in Table 1.

We first carried out the reaction using the Me_3SiCl–NaI–NEt_3 reagent in MeCN as described by Cazeau et al. (entry 1).[14] The reaction proceeds well at rt but the major product obtained was the less substituted enoxysilane **3a**. The reaction was also performed at 52 °C without improvement of the ratio **2a**:**3a**. To increase the proportion of the thermodynamic compound, other bases such as pyridine, lutidine and hexamethyldisilazane were tested using the same conditions (entries 2–5). Amongst the bases used, the best results were obtained when triethylamine was replaced by pyridine. In this case, the reaction, which led only to the thermodynamic compound **2a** as a mixture of *E*/*Z* diastereomers, was slower and required 36 h in MeCN at 52 °C for complete conversion (entry 2). When carried out in MeCN–pentane, the reaction was faster and gave more

Table 1. Conditions for enolisation of ketone **1a**–**e**, **1g**

Entry	Ketone	Solvent	*T* (°C)	Time (h)	Reagents	**2**:**3**[a]
1	**1a**	MeCN	rt	3	TMSCl, Et_3N, NaI	3:7
2	**1a**	MeCN	52	36	TMSCl, pyridine, NaI	1:0
3	**1a**	MeCN–pentane[b]	52	12	TMSCl, pyridine, NaI	1:0
4	**1a**	MeCN	52	24	TMSCl, lutidine, NaI	4:1
5	**1a**	MeCN	52	24	TMSCl, HMDS, NaI	7:3
6	**1a**	DMF	100	36	TMSCl, NEt_3	1:0
7	**1b**	MeCN–pentane[b]	rt	12	TMSCl, pyridine, NaI	9:1
8	**1c**	MeCN–pentane[b]	52	12	TMSCl, pyridine, NaI	9:1
9	**1c**	MeCN–cyclohexane[b]	70	12	TMSCl, pyridine, NaI	1:0
10	**1d**	MeCN–cyclohexane[b]	52	12	TMSCl, pyridine, NaI	1:0
11	**1e**	MeCN–cyclohexane[b]	70	12	TMSCl, pyridine, NaI	23:2
12	**1g**	MeCN–cyclohexane[b]	70	12	TMSCl, pyridine, NaI	1:0

[a] Determined by ^1H NMR on the crude mixture.
[b] In a 6:5 ratio.

reproducible results (entry 3). The reaction was also performed using the conditions described by House with trimethylsilyl chloride in the presence of triethylamine in DMF at 100 °C for 36 h (entry 6).[15] A complete conversion as well as a complete regioselectivity in favour of the thermodynamic compound was obtained but these conditions gave less reproducible results, which led us to prefer the conditions described in entry 3.

Once obtained, the resulting enoxysilane **2a** was directly engaged (without purification) in an oxidation reaction with ozone at −78 °C in CH_2Cl_2. Under these conditions, moderate yields of the aldehyde were obtained (40–50%). To improve these results, we decided to perform the oxidation in a two-step sequence. The enoxysilane was then transformed into the α-hydroxyketone **4a** by a freshly prepared solution of dimethyldioxirane (DMDO).[16] Since the enoxysilane is quite sensitive to acidic conditions, the reaction was carried out in the presence of potassium carbonate (0.5 equiv) and led to **4a** along with its *O*-silylated form (5%) that gave after acidic treatment pure **4a** in a good 85% yield as a 9:1 mixture of diastereomer. The major diastereomer could be isolated by recrystallisation in EtOAc and the absolute configuration at C-1 (*R*) of the newly formed stereocentre was determined by X-ray diffraction (Fig. 1). This major configuration could be explained by the preferential formation of the epoxide on the alpha face (*Si* face) of the enoxysilane that is less sterically hindered.

It also worth to be noticed that other oxidants such as *m*-CPBA or oxone were less efficient or led to degradation of the acidic labile enoxysilane.

Further treatment of α-hydroxyketone **4a** with sodium metaperiodate in THF–water provided the desired aldehyde **6a**. Due to its instability and to achieve better purification by column chromatography, the product was protected and stored as aminal **7a** in 77% yield from **4a**. Aminal **7a** could also be obtained in 68% overall yield from ketone **1a** after a single purification by column chromatography at the end of the synthesis. This four-step sequence could be performed on multigram scale (7 g of ketone **1a**). The deprotection of the aminal function with Dowex H^+ resin led quantitatively to **6a**, which can be used directly without further purification. It is also worth to note that, under these deprotection conditions, the anomeric integrity of the aldehyde is maintained and only the β-form is obtained.

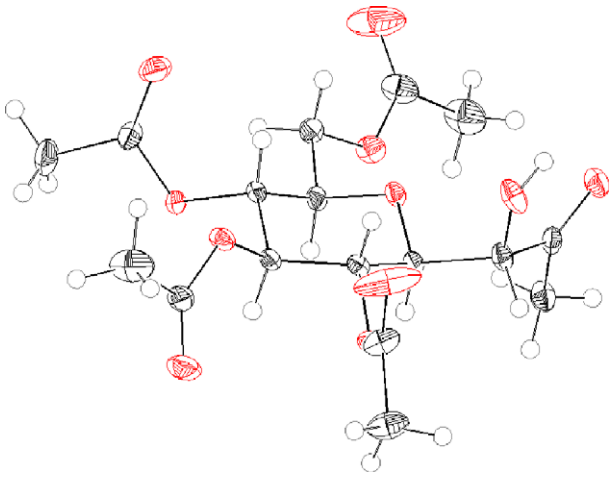


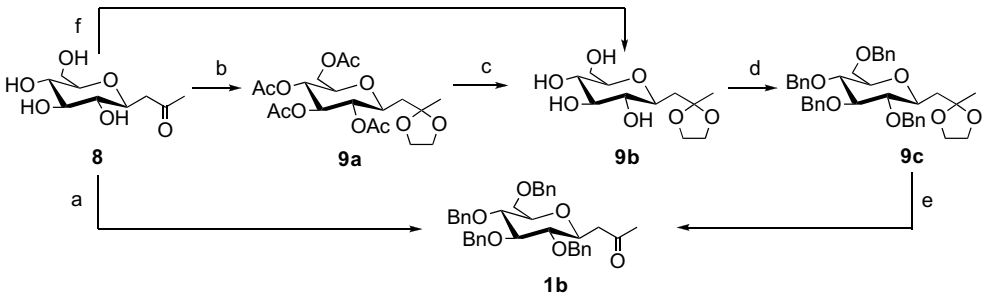
Figure 1. ORTEP drawing of **4a**. Ellipsoids are drawn at the 50% probability level.

The synthesis of 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosylformaldehyde **6b** was more challenging since obtaining *O*-benzylated ketone **1b** directly from **8** proved to be non-trivial (Scheme 2). With the classical benzylation method (NaH, DMF and BnBr), a complex mixture was obtained whereas no reaction was observed under milder conditions. Only the use of Ag_2O in DMF allowed us to obtained the desired compound **1b**. This reaction required 8 equiv of the expensive Ag_2O and only poor yields (30–45%) were observed. We decided then to synthesise ketone **1b** in a four-step sequence from **1a**: this latter was first protected with ethylene glycol in toluene, then deacetylation (MeONa in MeOH), followed by benzylation with NaH in DMF and removal of intermediate cyclic ketal gave **1b** in 83% overall yield from **1a**. Only a final purification was necessary to obtain multigrams of ketone **1b**. A shorter synthesis of **1b** can also be performed from **8**, which can be directly protected with ethylene glycol in a mixture of benzene–MeCN. Benzylation and deprotection of the cyclic ketal furnished the desired compound in 69% yield over three steps.

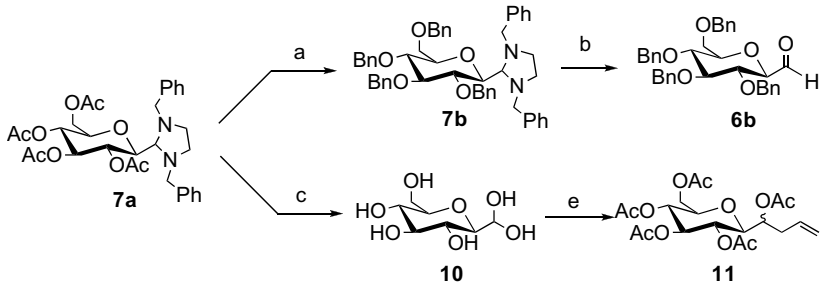
The enolisation reaction was carried out as described above, albeit at rt since degradation was observed with heating at 52 °C (Table 1, entry 7). In these conditions, the formation of the thermodynamic product **2b** was observed along with a minor quantity of the kinetic compound **3b** (in a 9:1 ratio). The crude mixture of enoxysilanes was then oxidised with dimethyldioxirane affording a mixture of hydroxyketones **4b** and **5b** in 72% yield after purification. After treatment with sodium periodate, aldehyde **6b** was isolated by column chromatography in 90% yield. In this case, the aldehyde is stable enough to be stored without protection for few months in the freezer.

Alternatively and in a simpler manner, 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosylformaldehyde **6b** could be prepared in a three-step procedure from aminal **7a** (Scheme 3). After deacetylation (NaOMe in MeOH) and benzylation with NaH in DMF, **7b** was obtained in 90% yield over two steps. The deprotection of the aminal with Dowex H^+ resin led to **6b**, which was isolated in 94% yield after purification.

The synthesis of aminal **7a** also allowed us to prepare the free hydrated aldehyde **10**[17] (Scheme 3). This was achieved by simple acetate deprotection (NaOMe in MeOH) followed by removal of the aminal function (Dowex H^+). For proof of structure of aldehyde **10**,



Scheme 2. Reagents and conditions: (a) BnBr, Ag_2O, DMF (**1b**, 30–45%); (b) (i) Ac_2O, pyridine (**1a**, 91%); (ii) ethylene glycol, toluene, PPTS (**9a**); (c) MeONa, MeOH (**9b**); (d) BnBr, NaH, DMF (**9c**); (e) TFA–water (**1b**); (f) ethylene glycol, benzene–MeCN, PPTS (**9b**).



Scheme 3. Reagents and conditions: (a) (i) NaOMe, MeOH; (ii) NaH, BnBr, DMF (**7b**, 90%); (b) Dowex H^+ resin, water–THF (**6b**, 94%); (c) (i) NaOMe, MeOH; (ii) Dowex H^+ resin, water–THF (**10**); (e) (i) allyl bromide, In, water–THF; (ii) Ac_2O, pyridine (**11**, 85% over 4 steps).

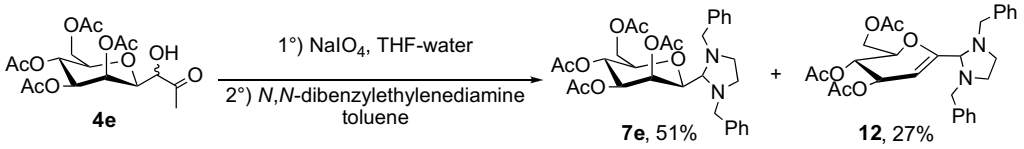
it was allowed to react in a 1:1 mixture of THF–water in the presence of allyl bromide and indium. After acetylation of the reaction mixture, **11** was obtained as a 7:3 mixture of diastereomers and in 85% yield over four steps.

We then extended the methodology to other pyranose derivatives such as D-galactose and lactose. In the case of ketone **1c**[18] derived from D-galactose (Scheme 1), we reproduced first the conditions of enolisation described for the D-glucose series. However, a mixture of thermodynamic enol **2c** and kinetic one **3c** was obtained in a 9:1 ratio (Table 1, entry 8). To diminish the formation of the latter, the reaction was carried out at higher temperature (70 °C) by replacing pentane by cyclohexane. Using the biphasic MeCN–cyclohexane solvent, the thermodynamic compound was the sole product obtained in a quantitative way (Table 1, entry 9). The oxidation of the trimethylsilyl enol ether with DMDO provided the resulting α-hydroxyketone **4c**, which was obtained as a 9:1 mixture of two diastereomers. After treatment with sodium periodate in THF–water, aldehyde **6c** was protected as an aminal that was obtained in 65% overall yield from ketone **1c**.

For ketone **1d**, derived from lactose, the enolisation step was carried out at 52 °C with the TMSCl–NaI–pyridine system in MeCN–pentane and led only to the thermodynamic compound **2d** in a quantitative manner (Table 1, entry 10). After treatment with DMDO, the α-hydroxyketone **4d** is obtained as a 4:1 mixture of diastereomers. Then, the cleavage with sodium periodate and protection of the resulting aldehyde **6d** with *N*,*N*-dibenzylethylenediamine allowed the obtention of aminal **7d** in 70% yield.

It is worth to be noticed that a limitation to our strategy was found for the synthesis of aldehyde derived from D-mannose. In this case, the enolisation of ketone **1e** at 52 °C in MeCN–pentane led to an incomplete reaction. The reaction was then carried out at 70 °C and the desired product was obtained along with some kinetic product (Table 1, entry 11). Then, the oxidation reaction with DMDO led to a mixture of diatereomeric α-hydroxyketones **4e** along with **5e** (Scheme 1). However, **4e** could be isolated after flash chromatography in 69% yield and in a 14:11 diastereomeric ratio. The difficulty was found after treatment of **4e** with $NaIO_4$ then protection of the resulting aldehyde as an aminal. This latter was found to be very sensitive to elimination and after flash chromatography, we obtained a mixture of the desired aminal **7e** and adduct **12** that are difficult to separate (Scheme 4).

This methodology could be extended to the preparation of the highly-coveted GlcNAc 1-formyl derivatives[10b,19] from 2′-acetamido-2′-deoxy-3′,4′,6′-tri-*O*-acetyl-β-D-glucopyranosylpropane-2-one **1f**.[20] The synthesis of *C*-glycosyl compounds of GlcNAc is of particular interest since amino sugars are widely



Scheme 4. Oxidative cleavage of α-hydroxyketone **4e**.

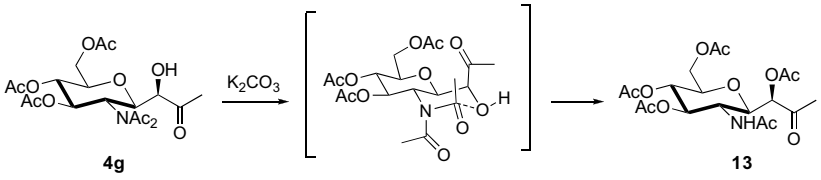
distributed in biological systems and are fundamental constituents of glycoproteins, a class of natural products with crucial roles in biological recognition phenomena.[21]

In the first instance, the enolisation of ketone **1f**[18] was studied. However, under various conditions, no reaction was observed. A second acetate group was then introduced onto the nitrogen centre by treating **1f** with isopropenyl acetate in the presence of APTS to afford the *N*,*N*-diacetate derivative **1g** in a quantitative yield (Scheme 1). Using the conditions described for the D-glucose series, the enolisation of ketone **1g** with the Me_3SiCl–NaI–pyridine system at 52 °C in a mixture of MeCN–pentane was not complete. However, when pentane was replaced by cyclohexane to perform the reaction at 70 °C, a complete conversion was observed (Table 1, entry 12). Moreover, the thermodynamic enoxysilane **2g** was the sole compound obtained as a mixture of *E*/*Z* stereoisomers that was directly engaged in the oxidation reaction using dimethyldioxirane. The reaction was first carried out in the presence of potassium carbonate (0.5 equiv) as described for other sugar derivatives. In this case, we obtained a mixture of α-hydroxyketones **4g** and **13** in a 3:2 ratio (Scheme 5). The formation of **13** may be explained by the internal migration of one acetate group from the nitrogen atom to the free alcohol at the C-1 position probably through a six-membered transition state. This problem was solved when the reaction was performed in the absence of potassium carbonate and after flash chromatography the desired α-hydroxyketone **4g** was obtained in 70% yield as a single diastereomer.

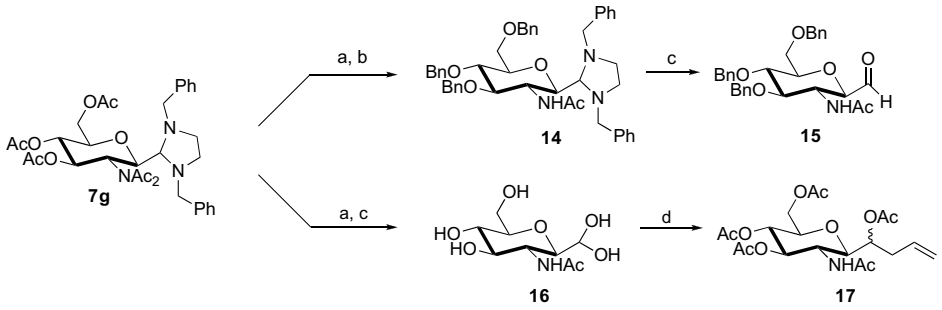
Further treatment with sodium metaperiodate in THF–water provided aldehyde **6g**, which was converted for storage into aminal **7g** in 65% overall yield from **1g**.[20] Aldehyde **6g** can be regenerated by simple treatment with Dowex H^+ resin and can be used directly without further purification. Aldehyde **6f** can be synthesised in a two-step sequence from **6g** by Zemplèn deacetylation then reacetylation (Ac_2O, pyridine) to afford the desired compound in 68% yield after purification. The synthesis of aldehyde **6f** could also be achieved by treatment of aminal **7g** with hydrazine monohydrate in a mixture of MeOH–THF as described by Burk and Allen.[22] However, using these conditions, some decomposition occurred and aminal **7f** was obtained in only 54% yield. In contrast, performing the reaction in pure CH_2Cl_2 allowed us to obtain aminal **7f** in 88% yield (Scheme 1). The deprotection of the aminal function with Dowex H^+ resin led quantitatively to **6f**, which can be used without purification.

Aminal **7g** can also serve as a precursor of other aldehydes such as the benzylated aldehyde **14** and the free hydrated aldehyde **16** (Scheme 6). Indeed, after deacetylation of **7g** (NaOMe in MeOH), a benzylation step carried out with NaH in DMF produced **14** in 75% yield over two steps. Further treatment of **14** with Dowex H^+ resin gave the desired aldehyde **15** quantitatively. Finally, the synthesis of **16** was achieved after deprotection of the alcohols directly followed by removal of the aminal function. Compound **16** was found to be rather unstable and was not isolated but for proof of efficiency it was allowed to react with allylbromide in the presence of indium in a 1:1 mixture of THF–water. After acetylation of the reaction mixture, the allylated compound **17** was obtained as a 3:1 mixture of diastereomers in 87% yield over four steps.

In summary, we reported an efficient synthesis of synthetically useful β-*C*-glycosylformaldehydes from easily available *C*-glycosyl-propanones. Our strategy allows the direct access to peracetylated glycosylformaldehydes such as 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylformaldehyde (five steps, 57% overall yield from D-glucose), 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosylformaldehyde (five steps, 58% overall yield from D-galactose) or peracetylated lactopyranosyl formaldehyde (five steps, 57% overall yield from lactose). An alternative to the preparation of perbenzylated derivatives from the peracetylated compounds can be achieved by simple protection–deprotection sequences. This methodology,



Scheme 5. Formation of **13** by acetate migration.



Scheme 6. Reagents and conditions: (a) NaOMe, MeOH; (b) NaH, BnBr, DMF (**14**, 75%); (c) Dowex H^+ resin, water–THF; (d) (i) allyl bromide, In, water–THF; (ii) Ac_2O, pyridine (**17**, 87% over 4 steps).

which does not require the use of the hardly available perbenzyl glyconolactone, allowed us to prepare 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosylformaldehyde in nine steps (50% overall yield from D-glucose). The methodology was then efficiently applied to the preparation and synthetically useful protected or unprotected 2-acetamido-2-deoxy-β-D-glucopyranosylformaldehydes in good yields. Further applications of the above method for the synthesis of more complex *C*-glycosyl compounds or *C*-disaccharides of biological relevance will be presented in due course.

3. Experimental

3.1. General methods and materials

All moisture sensitive reactions were performed under argon using oven-dried glassware. If necessary, solvents were dried and distilled prior to use. Reactions were monitored on Silica Gel plates 60 F_{254} (E. Merck). Detection was performed using UV light and/or 5% H_2SO_4 in EtOH, followed by heating. Flash chromatography was performed on silica gel 6–35 μm. ^1H and ^{13}C NMR spectra were recorded at rt with Bruker AC 200, 250 or AM 400 spectrometers. Chemical shifts are reported in δ versus Me_4Si for ^1H NMR spectra (external reference for D_2O) and relative to the $CDCl_3$ resonance at 77.00 ppm for ^{13}C NMR spectra in $CDCl_3$ and relative to Me_4Si for ^{13}C NMR spectra in D_2O. Melting points were measured on a Büchi Melting Point B-545 apparatus. Optical rotations were measured on an Electronic Digital Jasco DIP-370 Polarimeter. Mass spectra were recorded in positive mode on a Finnigan MAT 95 S spectrometer using electrospray ionisation. Elemental analyses were performed at the Service Central de Microanalyses du CNRS (Gif-sur-Yvette, France). It is worth to note that the percent oxygen values are measured with Elementar apparatus using pyrolysis and catharometric detection.

X-ray diffraction data for **4a** were collected by using a Kappa X8 APPEX II Bruker diffractometer with graphite-monochromated $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å). The temperature of the crystal was maintained at the selected value (180 K) by means of a 700 series Cryostream cooling device to within an accuracy of ±1 K. The data were corrected for Lorentz, polarisation and absorption effects. The structures were solved by direct methods using SHELXS-97 and refined against F^2 by full-matrix least-squares techniques using SHELXL-97 with anisotropic displacement parameters for all non-hydrogen atoms. Hydrogen atoms were located on a difference Fourier map and introduced into the calculations as a riding model with isotropic thermal parameters. All calculations were performed by using the Crystal Structure crystallographic software package WINGX. The absolute configuration was determined by refining the Flack's parameter using a large of Friedel's pairs. The drawing of the molecule was realised with the help of ORTEP32.

3.2. General procedure A: enolisation of ketone (1a–e) and (1g)

To a soln of ketone in 6:5 MeCN–solvent were added pyridine, TMSCl and then sodium iodide. The soln was stirred under argon for 12 h at T °C. The reaction was poured into satd aq $NaHCO_3$ (15 mL) and extracted with EtOAc (3 × 15 mL). The combined organics layers were washed with brine (15 mL), dried (Na_2SO_4), filtered and concentrated to afford the crude enoxysilane, which was used without further purification.

3.3. General procedure B: synthesis of α-hydroxyketone (4a–e), (5b) and (5e)

To a mixture of the crude enol ether (2 mmol) and potassium carbonate (0.5 equiv) was added a soln of dimethyldioxirane (0.1 M in acetone, 3 equiv). The soln was stirred for 3 h at rt, filtered and concentrated. The residue was dissolved in 3:1 THF–water (4 mL) and aq HCl (1.5 N, 1 mL) was added. After stirring for 1 h, the soln was neutralised with satd aq $NaHCO_3$. Brine

(15 mL) was added and the aq phase was extracted with EtOAc (3×15 mL), dried ($MgSO_4$), concentrated and purified by flash chromatography.

3.4. General procedure C: synthesis of aminals (7a–e), (7g)

To a soln of α-hydroxyketone (0.5 mmol) in 3:4 THF–water (3.5 mL) was added sodium metaperiodate. The mixture was stirred at rt and neutralised with satd aq $NaHCO_3$. After addition of brine (10 mL) the aq phase was extracted with EtOAc (3×10 mL). The combined organic phases were washed with brine (2×15 mL), dried (Na_2SO_4), filtrated and concentrated. After work-up, toluene (10 mL) and *N*,*N*-dibenzylethylenediamine (1.05 equiv) were added to the crude aldehyde. The soln was concentrated under diminished pressure and toluene (2×10 mL) was added and evaporated. Pure aminal was obtained after flash chromatography.

3.5. General procedure D: synthesis of aldehydes (6a–d) and (6g)

To a soln of the aminal (0.3 mmol) in 1:1 THF–water (2 mL) was added Dowex H^+ resin and the suspension was stirred for 4 h at rt. After filtration and concentration, the residue was used directly (**6a**, **6c**,**d** and **6f**,**g**) or purified by flash chromatography (**6b**).

3.6. 4,8-Anhydro-5,6,7,9-tetra-*O*-benzyl-1,3-dideoxy-D-*glycero*-D-*gulo*-non-2-ulose (1b)

3.6.1. Procedure 1. A soln of **1a** (500 mg, 1.3 mmol) and ethylene glycol (145 μL, 2.6 mmol) in toluene (10 mL) containing a catalytic amount of PPTS (50 mg, 0.2 mmol) was refluxed while water was continuously removed by means of a Dean Stark trap. After 8 h, toluene was removed under diminished pressure and replaced by CH_2Cl_2 (15 mL). Satd aq $NaHCO_3$ (15 mL) was added and the product was extracted with CH_2Cl_2 (3×15 mL). The combined organic phases were washed with brine (30 mL), dried ($MgSO_4$) and concentrated to afford crude **9a**. ^{1}H NMR (250 MHz, $CDCl_3$): δ (ppm) 1.30 (s, 3H, H-1), 1.65 (dd, 1H, $J_{3a,3b}$ 12, $J_{3a,4}$ 1 Hz, H-3a), 1.75 (dd, 1H, $J_{3a,3b}$ 12, $J_{3b,4}$ 7 Hz, H-3b), 1.86–2.05 (m, 12H, CO_2CH_3), 3.52–3.64 (m, 2H, H-8 and H-4), 3.75–3.90 (m, 4H, OCH_2CH_2O), 4.01 (dd, 1H, $J_{9a,8}$ 2.5 and $J_{9a,9b}$ 12.5 Hz, H-9a), 4.11 (dd, 1H, $J_{9b,8}$ 6 and $J_{9b,9a}$ 12.5 Hz, H-9b), 4.76 (t, 1H, $J_{5,6} = J_{5,4}$ 9 Hz, H-5), 4.92 (t, 1H, $J_{7,6} = J_{7,8}$ 9 Hz, H-7), 5.08 (t, 1H, $J_{6,5} = J_{6,7}$ 9 Hz, H-6); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ (ppm) 20.2, 20.3 ($4 \times CO_2CH_3$), 24.2 (C-3), 39.5 (*C*-1), 62.2 (C-9), 64.1 (OCH_2CH_2O), 68.4, 73.9, 74.4, 75.1 (C-4, C-5, C-6, C-7, C-8), 108.3 (C-2), 169.1, 169.3, 169.8, 170.1 ($4 \times CO_2CH_3$). The crude residue was dissolved in MeOH (10 mL) and a catalytic amount of sodium methoxide (30 mg) was added. The suspension was stirred for 8 h at rt and concentrated to afford **9b**. ^{1}H NMR (250 MHz, D_2O): δ (ppm) 1.35 (s, 3H, CH_3–CO), 1.75 (dd, 1H, $J_{3a,4}$ 10 and $J_{3a,3b}$ 12 Hz, H-3a), 2.20 (d, 1H, $J_{3b,3a}$ 16 Hz, H-3b), 3.10 (t, 1H, $J_{5,4} = J_{5,6}$ 10 Hz, H-5), 3.25–3.45 (m, 4H, H-4, H-5, H-6 and H-7), 3.65 (dd, 1H, $J_{9a,8}$ 5, $J_{9a,9b}$ 12 Hz, H-9a), 3.83 (d, 1H, $J_{9b,9a}$ 12 Hz, H-9b), 3.98 (s, 4H, OCH_2CH_2O); ^{13}C NMR (62.5 MHz, D_2O): δ (ppm) 24.0 (C-1), 39.8 (C-3), 61.3 (C-9), 64.5, 64.8 (OCH_2CH_2O), 70.2, 73.6, 76.4, 77.8, 79.9 (C-4, C-5, C-6, C-7, C-8), 109.8 (C-2). The crude residue was dissolved in anhyd DMF (13 mL) and sodium hydride (60% dispersion in mineral oil, 262 mg, 7.8 mmol) was added portionwise. The soln was stirred for 20 min at rt and benzyl bromide (0.8 mL, 7.8 mmol) was introduced over a period of 10 min. After 2 h, MeOH (0.5 mL) was added. Water (20 mL) was introduced and the aq phase was extracted with EtOAc (3×20 mL). The combined organic layers were washed with water (2×20 mL) then brine (20 mL) and dried ($MgSO_4$). After concentration, crude **9c** was obtained. Mp 91–92 °C; $[\alpha]_D^{25}$ −9.3 (*c* 1, $CHCl_3$); ν_{max} (thin film): 2871, 1496, 1454, 1360, 1099, 1028, 735, 697 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ (ppm) 1.45 (s, 3H, CH_3CO), 1.75 (dd, 1H, $J_{3,4}$ 9, $J_{3a,3b}$ 14 Hz, H-3a), 2.10 (d, 1H, $J_{3b,3a}$ 14 Hz, H-3b), 3.28 (t, 1H, $J_{5,4} = J_{5,6}$ 9 Hz, H-5), 3.40–3.55 (m, 2H, H-4 and H-8), 3.60–3.77 (m, 4H, H-6, H-7, H-9a and H-9b), 3.84–3.94 (m, 4H, OCH_2CH_2O), 4.57–4.69 (m, 4H, CH_2-Ph), 4.82–4.99 (m, 4H, CH_2-Ph), 7.15–7.35 (m, 20H, Ph); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ (ppm) 24.9 (C-1), 39.7 (C-3), 64.4 (OCH_2CH_2O), 69.0 (C-9), 73.4, 74.9, 75.1, 75.5 (CH_2-Ph), 76.3 (C-4), 78.5 (C-7), 78.6 (C-8), 81.9 (C-5), 87.3 (C-6), 109.2 (C-1), 127.5, 127.6, 127.7, 127.8, 127.9, 128.3, 128.4 (Ph); ESIMS: $m/z = 647$ $(M+Na)^+$; Anal. Calcd for $C_{39}H_{44}O_7$: C, 74.98; H, 7.10; O, 18.92. Found: C, 74.91; H, 7.09. Finally, the residue was dissolved in TFA (3 mL), water (200 μL) was added and the mixture was stirred at rt for 30 min. The soln was poured into cold satd aq $NaHCO_3$ (10 mL). The organic phase was extracted with EtOAc (3×15 mL), the combined organic layers were washed with brine (15 mL) and dried ($MgSO_4$). After concentration, the product was purified by flash chromatography (9:1→4:2 petroleum ether–EtOAc) to afford the desired compound **1b** as a white solid (625 mg, 83% over 4 steps). Mp 70–72 °C; $[\alpha]_D^{25}$ −2.2 (*c* 1, $CHCl_3$); ν_{max} (thin film): 2871, 1716, 1496, 1454, 1359, 1090, 1028, 736, 698 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ (ppm) 2.16 (s, 3H, C-1), 2.60 (dd, 1H, $J_{3a,4}$ 8, $J_{3a,3b}$ 16 Hz, H-3a), 2.70 (dd, 1H, $J_{3b,4}$ 4, $J_{3b,3a}$ 16 Hz, H-3b), 3.38 (m, 1H, H-8), 3.45–3.55 (m, 1H, H-4), 3.64–3.89 (m, 4H, H-9a, H-9b and CH_2-Ph), 4.5–5.1 (m, 9H, H-5, H-6, H-7 and $3 \times CH_2$-Ph), 7.2–7.5 (m, 20H, $4 \times$ Ph); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ (ppm) 31.3 (C-1), 45.8 (C-3), 68.6 (C-9),

73.3, 74.82, 74.85, 75.4 (4 × CH_2-Ph), 75.4, 78.2, 78.8, 81.1 (C-5, C-6, C-7, C-8), 87.0 (C-4), 127.5, 127.6, 127.7, 127.8, 128.2, 128.3, 128.32 (C=H Ph), 137.84, 137.91, 137.98, 138.3 (Cq Ph), 206.4 (C-2); ESIMS: $m/z = 603$ $(M+Na)^+$; Anal. Calcd for $C_{37}H_{40}O_6$: C, 76.53; H, 6.94; O, 16.53. Found: C, 76.74; H, 7.03; O, 16.45.

3.6.2. Procedure 2. A soln of **8**[11] (220 mg, 1 mmol) and ethylene glycol (130 μL, 2.2 mmol) in 1:1 benzene–MeCN (6 mL) containing a catalytic amount of PPTS (50 mg, 0.2 mmol) was refluxed while water was continuously removed by means of a Dean Stark trap. After 20 min, benzene was eliminated, aq NaOH (0.03 M, 10 mL, 0.3 mmol) was introduced and the soln was concentrated under diminished pressure. The crude residue was purified by flash chromatography (5:3:1 EtOAc–*i*-PrOH–water) to afford **9b**. Compound **9b** was dissolved in anhyd DMF (3 mL) and sodium hydride (60% dispersion in mineral oil, 400 mg, 10 mmol) was added portionwise. The soln was stirred for 20 min at rt before benzyl bromide (1.2 mL, 10 mmol) was added over a period of 10 min. The reaction was completed in 2 h and MeOH (1 mL) was added. After addition of water (10 mL), the aq phase was extracted with EtOAc (3 × 20 mL). The combined organics phases were washed with water (2 × 20 mL) then brine (20 mL), dried (Na_2SO_4), filtered and concentrated. Flash chromatography (4:1 petroleum ether–EtOAc) gave the desired product **9c** (437 mg, 70%). Finally, the product was dissolved in TFA (3 mL), water (200 μL) was added and the mixture was stirred at rt for 30 min. The soln was poured into satd aq $NaHCO_3$ (10 mL). The aq phase was extracted with EtOAc (3 × 15 mL), the combined organic layers were washed with brine (15 mL) and dried ($MgSO_4$). After concentration, the product was purified by flash chromatography (9:1→4:1 petroleum ether–EtOAc) to afford the desired compound **1b** as a white solid (400 mg, 69% over 3 steps). The NMR data were identical to those previously obtained with procedure 1.

3.7. Synthesis of 3,4,5,7-tetra-*O*-benzyl-2,6-anhydro-D-*glycero*-D-*gulo*-heptose (6b) from 1b

The enolisation reaction was performed on ketone **1b** (780 mg, 2 mmol) according to general procedure A using pyridine (480 μL), TMSCl (760 μL) and then NaI (900 mg) in 6:5 MeCN–pentane (5.5 mL) at rt. After treatment, the oxidation reaction was performed with DMDO (30 mL, 1.5 equiv) according to general procedure B. Flash chromatography (17:3→7:3 petroleum ether–EtOAc) led first to the major diastereoisomer of **4b** then a mixture of the minor isomer of **4b** with **5b** (0.858 g, 72%). For the major isomer: white solid, mp 108–109 °C; $[\alpha]_D^{25}$ +46.6 (*c* 1, $CHCl_3$); ν_{max} (thin film): 3425, 2870, 1716, 1454, 1360, 1103, 736, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.25 (s, 3H, C-1), 3.46 (m, 1H, H-8), 3.58 (t, 1H, $J_{7,6} = J_{7,8}$ 9.5 Hz, H-7), 3.59–3.65 (m, 1H, H-9a), 3.64 (dd, 1H, $J_{9b,8}$ 1.7 and $J_{9b,9a}$ 11 Hz, H-9a), 3.72 (dd, 1H, $J_{4,3}$ 2.5 and $J_{4,5}$ 9.5 Hz, H-4), 3.77 (t, 1H, $J_{6,5} = J_{6,7}$ 9.5 Hz, H-6), 3.89 (t, 1H, $J_{5,6} = J_{5,4}$ 9.5 Hz, H-5), 4.42–4.46 (br s, 1H, H-3), 4.47–4.58 (m, 2H, CH_2-Ph), 4.62 (d, 1H, *J* 11 Hz, CH_2-Ph), 4.82–4.89 (m, 2H, CH_2-Ph), 4.93–5.02 (m, 3H, CH_2-Ph), 7.15–7.45 (m, 20H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 25.4 (C-1), 69.0 (C-9), 73.4, 75.2, 75.3, 75.7 (CH_2-Ph), 76.9 (C-3), 78.2 (C-5), 78.3 (C-7), 79.2 (C-4), 79.9 (C-8), 87.0 (C-6), 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.4, 128.5, 128.6 (Ph), 138.1, 138.3, 138.4, 138.7 (Cq Ph), 207.1 (C-2); ESIMS: $m/z = 619$ $(M+Na)^+$; Anal. Calcd for $C_{37}H_{40}O_7$: C, 74.47; H, 6.76; O, 18.77. Found: C, 74.56; H, 6.91; O, 18.76.

Aldehyde **6b** was obtained according to general procedure C. The reaction was performed on 0.3 g of the mixture of **4b** and **5b** using $NaIO_4$ (1 g, 4.5 mmol, 9 equiv) for 18 h. After work-up, the residue was purified by flash chromatography (4:1 petroleum ether–EtOAc + 0.1% Et_3N) to afford the pure aldehyde **6b** (248 mg, 90%). The NMR data were consistent with those reported in the literature.[9]

3.8. 3,4,5,7-Tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-L-*manno*-heptose (6c)

The enolisation reaction was performed on ketone **1c** (94 mg, 0.5 mmol) according to general procedure A using pyridine (160 μL), TMSCl (260 μL) and then NaI (300 mg) in 6:5 MeCN–cyclohexane (1.37 mL) at 70 °C. After work-up, general procedure B was applied to the crude enol ether **2c** (0.5 mmol) using DMDO (15 mL, 3 equiv) and K_2CO_3 (34.5 mg). Flash chromatography (7:3 petroleum ether–EtOAc) gave **4c** as a colourless oil (133 mg, 66% from **1c**). $[\alpha]_D^{25}$ +5 (*c* 1, $CHCl_3$); ν_{max} (thin film): 1758, 1371, 1230, 1053 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$): δ (ppm) 2.00 (s, 3H, CO_2CH_3), 2.02 (s, 3H, CO_2CH_3), 2.05 (s, 3H, CO_2CH_3), 2.17 (s, 3H, CO_2CH_3), 2.29 (s, 3H, C-1), 3.87–3.92 (m, 2H, H-4 and H-8), 4.01–4.15 (m, 3H, H-9a, H-9b and H-3), 5.12 (dd, 1H, $J_{6,7}$ 3 and $J_{6,5}$ 10 Hz, H-6), 5.38–5.50 (m, 2H, H-5 and H-7); ^{13}C NMR (90 MHz, $CDCl_3$): δ (ppm) 20.6, 20.7, 20.8 (4 × CO_2CH_3), 26.2 (C-1), 61.4 (C-9), 65.9, 67.4 (C-5, C-7), 71.9 (C-6), 73.8 (C-3), 74.7 (C-8), 75.1 (C-4), 170.1, 170.3 (CO_2CH_3), 207.4 (C-2); ESIMS: $m/z = 427$ [$(M+Na)^+$, 100%], ESIHRMS: m/z 427.1202. $C_{17}H_{24}O_{11}Na_1$ requires 427.1211.

Aminal **7c** was then synthesised according to general procedure C. The reaction was performed with crude **4c** (0.5 mmol) using $NaIO_4$ (341 mg) for 3 h. After work-up then treatment with *N*,*N*-dibenzylethylenediamine, **7c** (colourless oil, 213 mg, 70% from **1c**) was obtained after flash chromatography (4:1 petroleum

ether–EtOAc + 0.1% Et_3N). $[\alpha]_D^{25}$ +9.2 (*c* 1, $CHCl_3$); ν_{max} (thin film): 3054, 2986, 1748, 1265, 739, 705 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$): δ (ppm) 1.86 (s, 3H, CO_2CH_3), 1.90 (s, 3H, CO_2 CH_3), 1.96 (s, 3H, CO_2 CH_3), 1.97 (m, 3H, CO_2 CH_3), 2.33–2.44 (m, 1H, N–C*H*2–), 2.45–2.53 (m, 1H, N–C*H*2–), 2.75–2.83 (m, 1H, N–C*H*2–), 2.93 (dt, 1H, *J* 5.5 Hz, *J* 7.5 Hz, N–C*H*2–), 3.51 (d, 1H, *J* 13 Hz, CH_2-Ph), 3.56 (d, 1H, *J* 1 Hz, H-1), 3.58 (d, 1H, *J* 13 Hz, CH_2-Ph), 3.71 (dd, 1H, $J_{2,3}$ 9.5 Hz, $J_{2,1}$ 1.5 Hz, H-2), 3.88 (td, 1H, $J_{5,6}$ 1, $J_{6,7a} = J_{6,7b}$ 6 Hz, H-6), 4.01–4.07 (m, 2H, H-7a and CH_2-Ph), 4.11 (dd, 1H, $J_{7a,6}$ 6, $J_{7a,7b}$ 11 Hz, H-7b), 4.22 (d, 1H, *J* 13 Hz, CH_2-Ph), 5.12 (dd, 1H, $J_{4,5}$ 3.5 and $J_{4,3}$ 10 Hz, H-4), 5.41 (dd, 1H, $J_{5,6}$ 1, $J_{5,4}$ 3.5 Hz, H-5), 5.90 (t, 1H, $J_{3,4} = J_{3,2}$ 10 Hz, H-3), 7.20–7.50 (m, 10H, Ph); ^{13}C NMR (90 MHz, $CDCl_3$): δ (ppm) 20.5, 20.7, 20.7, 20.8, 21.1 (CH_3CO_2), 50.7 (CH_2–N), 50.9 (CH_2–N), 59.5 (CH_2-Ph), 59.8 (CH_2-Ph), 61.9 (C-7), 66.4 (C-3), 67.8 (C-5), 73.0 (C-4), 73.7 (C-6), 78.4 (C-2), 85.8 (C-1), 126.7, 127.1, 128.1, 128.2, 128.3, 128.4, 128.8 (Ph), 139.3, 140.0 (Cq Ph), 169.5, 170.3, 170.4 (CO); ESIMS: $m/z = 605$ [$(M+Na)^+$, 30%]; Anal. Calcd for $C_{31}H_{38}N_2O_9$: C, 63.90; H, 6.57; N, 4.81; O, 24.71. Found: C, 63.95; H, 6.87; N, 4.78; O, 24.59.

Using general procedure D, aldehyde **6c** was obtained: ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 2.00 (s, 3H, CO_2CH_3), 2.07 (s, 6H, $2 \times CO_2CH_3$), 2.17 (s, 3H, CO_2CH_3), 3.80 (dd, 1H, $J_{2,1}$ 2.0 Hz and $J_{2,3}$ 10.0 Hz, H-2), 4.01 (t, 1H, $J_{6,7a} = J_{6,7b}$ 7.0 Hz, H-6), 4.15–4.20 (m, 2H, H-7a and H-7b), 5.11 (dd, 1H, $J_{4,5}$ 3, $J_{4,3}$ 10.0 Hz, H-4), 5.36 (t, 1H, $J_{3,4} = J_{3,2}$ 10.0 Hz, H-3), 5.48 (d, 1H, $J_{5,4}$ 3.0 Hz, H-5), 9.58 (d, 1H, $J_{1,2}$ 2.0 Hz, H-1); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 20.5, 20.6 (CH_3CO_2), 61.7 (C-7), 62.6 (C-5), 67.3 (C-3), 71.3 (C-4), 74.5 (C-6), 80.5 (C-2), 169.8, 169.9, 170.1, 170.4 (CH_3CO_2), 196.0 (C-1).

3.9. 7-*O*-(β-D-2′,3′,4′,6′-Tetra-*O*-acetylgalactopyranosyl)-5,6,9-tri-*O*-acetyl-4,8-anhydro-1,3-dideoxy-D-*glycero*-D-*gulo*-non-2-ulose (1d)

To a soln of lactose monohydrate (0.5 g, 1.39 mmol) in 2:1 water–THF (9 mL) was added pentane-2,4-dione (0.28 mL, 2.77 mmol, 2 equiv) and $NaHCO_3$ (0.47 g, 5.56 mmol, 4 equiv). After heating at 90 °C for 36 h, the reaction mixture was neutralised with Dowex H^+ resin and filtrated. The aq phase was washed with CH_2Cl_2 (3×10 mL) and was concentrated under diminished pressure. After co-evaporation with toluene (3×10 mL), the residue was dissolved in 2:1 pyridine–Ac_2O (6 mL) and was stirred for 6 h at rt. After co-evaporation with toluene (3×10 mL), the residue was taken up in CH_2Cl_2 (15 mL) and was washed successively with satd aq $NaHCO_3$ (10 mL) and brine (10 mL) and dried ($MgSO_4$). After concentration, the product was purified by flash chromatography (11:9→2:3 heptane–EtOAc) to afford the desired compound **1b** as a white solid (0.78 g, 81% over 2 steps). Mp 79–81 °C; $[\alpha]_D^{25}$ −15.0 (*c* 1, $CHCl_3$); ν_{max} (thin film): 1739, 1369, 1218, 1041 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.93 (s, 3H, CH_3), 1.99 (s, 3H, CH_3), 2.00 (s, 3H, CH_3), 2.01 (s, 3H, CH_3), 2.04 (s, 3H, CH_3), 2.06 (s, 3H, CH_3), 2.12 (s, 3H, CH_3), 2.13 (s, 3H, CH_3), 2.42 (dd, 1H, $J_{3a,4}$ 3, $J_{3a,3b}$ 16 Hz, H-3a), 2.61 (dd, 1H, $J_{3b,4}$ 9, $J_{3b,3a}$ 16 Hz, H-3b), 3.57 (ddd, 1H, $J_{8,9a}$ 2, $J_{8,9b}$ 5, $J_{8,7}$ 10 Hz, H-8), 3.72 (t, 1H, $J_{7,8} = J_{7,6}$ 10 Hz, H-7), 3.84 (t, 1H, $J_{5',6'a} = J_{5',6'b}$ 7 Hz, H-5′), 3.89 (td, 1H, $J_{4,3a}$ 2, $J_{4,3b} = J_{4,5}$ 9 Hz, H-4), 4.01–4.14 (m, 4H, H-9b, H6′a and H-6′b), 4.37 (dd, 1H, $J_{9a,8}$ 2, $J_{9b,9a}$ 12 Hz, H-9b), 4.44 (d, 1H, $J_{1',2'}$ 8 Hz, H-1′), 4.77 (t, 1H, $J_{5,6} = J_{5,4}$ 9.5 Hz, H-5), 4.92 (dd, 1H, $J_{3',4'}$ 3, $J_{3',2'}$ 10.5 Hz, H-3′), 5.07 (dd, 1H, $J_{2',1'}$ 8, $J_{2',3'}$ 10.5 Hz, H-2′), 5.15 (t, 1H, $J_{6,5} = J_{6,7}$ 10 Hz, H-6), 5.31 (d, 1H, $J_{4',3'}$ 3 Hz, H-4′); ^{13}C NMR (90 MHz, $CDCl_3$): δ (ppm) 20.4, 20.5, 20.6, 20.7 ($7 \times CO_2CH_3$), 30.9 (C-1), 45.1 (C-3), 60.8 (C-6′), 62.1 (C-9), 66.6 (C-4′), 69.0 (C-2′), 70.6 (C-3′), 70.9 (C-5′), 71.8 (C-5), 73.6 (C-6), 73.8 (C-4), 76.3 (C-7), 77.6 (C-8), 100.9 (C-1′), 169.0, 169.9, 170.0, 170.1, 170.2, 170.3 (CO_2CH_3), 206.4 (C-2); ESIMS: $m/z = 699.3$ [$(M+Na)^+$, 100%]; Anal. Calcd for $C_{29}H_{40}O_{18}$: C, 51.48; H, 5.96; O, 42.56. Found: C, 51.11; H, 6.04; O, 42.65.

3.10. 5-*O*-(β-D-2′,3′,4′,6′-Tetra-*O*-acetylgalactopyranosyl)-3,4,7-tri-*O*-acetyl-2,6-anhydro-D-*glycero*-D-*gulo*-heptose (6d)

The enolisation reaction was performed on ketone **1d**[11] (304 mg, 0.45 mmol) according to general procedure A using pyridine (110 μL), TMSCl (172 μL) and then NaI (202 mg) in 6:5 MeCN–pentane (1.62 mL) at 52 °C. After work-up, general procedure B was applied to the crude enol ether **2d** (0.45 mmol) using DMDO (13.5 mL, 3 equiv) and K_2CO_3 (69 mg). Flash chromatography of the residue (1:1 petroleum ether–EtOAc) gave **4d** (white solid, 4:1 mixture of two diastereoisomers, 210 mg, 68% from **1d**). Mp 99–100 °C; ν_{max} (thin film): 1738, 1386, 1217, 1042 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) for the major diastereoisomer: δ (ppm) 1.95 (s, 3H, CH_3), 2.01 (s, 3H, CH_3), 2.05–2.08 (m, 12H, $4 \times CH_3$), 2.15 (s, 3H, CH_3), 2.25 (s, 3H, CH_3), 3.50 (d, 1H, OH), 3.57 (ddd, 1H, $J_{8,9a}$ 6, $J_{8,9b}$ 2, $J_{8,7}$ 10 Hz, H-8), 3.72 (t, 1H, $J_{7,8} = J_{7,6}$ 10 Hz, H-7), 3.84–3.91 (m, 2H, H-4 and H-5′), 4.01–4.14 (m, 4H, H-3, H6′a, H-6′b and H-9a,), 4.36 (dd, 1H, $J_{9b,8}$ 2, $J_{9b,9a}$ 12 Hz, H-9b), 4.47 (d, 1H, $J_{1',2'}$ 8 Hz, H-1′), 4.95 (dd, 1H, $J_{3',4'}$ 3, $J_{3',2'}$ 10.5 Hz, H-3′), 5.10 (dd, 1H, $J_{2',1'}$ 8, $J_{2',3'}$ 10.5 Hz, H-2′), 5.19 (t, 1H, $J_{5,6} = J_{5,4}$ 10 Hz, H-5), 5.26 (t, 1H, $J_{6,5} = J_{6,7}$ 10 Hz, H-6), 5.34 (dd, 1H, $J_{4',5'}$ 1, $J_{4',3'}$ 3 Hz, H-4′); ^{13}C NMR (90 MHz, $CDCl_3$): δ (ppm) 20.5, 20.6, 20.7, 20.8 ($7 \times CO_2CH_3$), 25.7 (C-1), 60.9 (C-6′), 62.2 (C-9), 66.6 (C-4′), 68.6

(C-5), 69.1 (C-2′), 70.7 (C-5′), 70.9 (C-3′), 74.0 (C-6), 74.8 (C-3), 76.4 (C-7), 77.2 (C-8), 77.5 (C-4), 101.1 (C-1′), 169.0, 169.9, 170.0, 170.1, 170.2, 170.3 (CO_2CH_3), 206.4 (C-2); ESIMS: $m/z = 715$ [$(M+Na)^+$, 100%]; ESI-HRMS: m/z 715.2047. $C_{29}H_{40}O_{19}Na_1$ requires 715.2056.

Aminal **7d** was then synthesised according to general procedure C. The reaction was performed with crude **4d** (0.45 mmol) using $NaIO_4$ (289 mg) for 2 h. After work-up then treatment with *N*,*N*-dibenzylethylenediamine, **7d** (amorphous solid, 213 mg, 70% from **1d**) was obtained after flash chromatography (13:7 petroleum ether–EtOAc + 0.05% Et_3N). $[\alpha]_D^{25}$ −8.2 (*c* 1, $CHCl_3$); ν_{max} (thin film): 2944, 1739, 1597, 1436, 1368, 1218, 1041, 908, 742, 704 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.86 (s, 6H, CO_2CH_3), 1.92 (s, 3H, CO_2 CH_3), 1.99 (s, 3H, CO_2 CH_3), 2.01 (s, 6H, CO_2 CH_3), 2.11 (s, 3H, CO_2 CH_3), 2.39 (td, 1H, *J* 7, *J* 9 Hz, N–C*H*2–), 2.51 (ddd, 1H, *J* 5, 7, 12 Hz, N–C*H*2–), 2.70–2.80 (m, 1H, N–C*H*2–), 2.87 (td, 1H, *J* 7, 9.5 Hz, N–C*H*2–), 3.44 (d, 1H, *J* 14 Hz, CH_2-Ph), 3.47–3.52 (m, 1H, H-6), 3.51 (d, 1H, *J* 1.5 Hz, H-1), 3.58 (d, 1H, *J* 14 Hz, CH_2-Ph), 3.68 (dd, 1H, $J_{2,3}$ 9 Hz, $J_{2,1}$ 1.5 Hz, H-2), 3.70 (t, 1H, $J_{5,6} = J_{5,4}$ 9 Hz, H-5), 3.83 (t, 1H, $J_{5',6'a} = J_{5',6'b}$ 7 Hz, H-5′), 3.88 (d, 1H, *J* 13 Hz, CH_2-Ph), 3.96 (dd, 1H, $J_{7a,6}$ 4 Hz, $J_{7a,7b}$ 12 Hz, H-7a), 3.98 (d, 1H, *J* 13 Hz, CH_2-Ph), 4.04 (dd, 1H, $J_{6'a,5'}$ 7.5 Hz, $J_{6'a,6'b}$ 11 Hz, H-6′a), 4.11 (dd, 1H, $J_{6'b-5'}$ 6.5 Hz, $J_{6'a,6'b}$ 11 Hz, H-6′b), 4.45 (d, 1H, $J_{1',2'}$ 8 Hz, H-1′), 4.52 (dd, 1H, $J_{7b,6}$ 2, $J_{7b,7a}$ 12 Hz, H-7b), 4.91 (dd, 1H, $J_{3',4'}$ 3, $J_{3',2'}$ 10.5 Hz, H-3′), 5.07 (dd, 1H, $J_{2',1'}$ 8, $J_{2',3'}$ 10.5 Hz, H-2′), 5.19 (t, 1H, $J_{3,2} = J_{3,4}$ 9 Hz, H-3), 5.29 (d, 1H, $J_{4',3'}$ 3 Hz, H-4′), 5.45 (t, 1H, $J_{4,3} = J_{4,5}$ 9 Hz, H-4), 7.10–7.40 (m, 10H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 20.5, 20.6, 20.9, 21.0 ($7 \times CO_2CH_3$), 50.7, 50.8 ($2 \times CH_2$–N), 59.2, 60.0 ($2 \times CH_2Ph$), 60.7 (C-6′), 61.9 (C-7), 66.6 (C-4′), 69.1 (C-2′), 69.5 (C-4), 70.5 (C-5′), 71.0 (C-3′), 75.0 (C-3), 76.3 (C-5, C-6), 78.1 (C-2), 85.1 (C-1), 101.1 (C-1′), 126.8, 127.1, 128.2, 128.3, 128.9 (*C*H Ph), 139.1, 139.8 (Cq Ph), 169.0, 169.7, 170.1, 170.2, 170.3 (CO_2CH_3); ESIMS: $m/z = 893.3$ [$(M+Na)^+$, 30%]; ESI-HRMS: m/z 893.3309; $C_{43}H_{54}O_{17}N_2Na_1$ requires 893.3315. Anal. Calcd for $C_{43}H_{54}N_2O_{17}$: C, 59.30; H, 6.25; N, 3.22; O, 31.23. Found: C, 59.25; H, 6.44; N, 3.21; O, 30.97.

Using general procedure D, aldehyde **6d** was obtained: ^1H NMR (400 MHz): δ (ppm) 2.05 (s, 3H, CO_2CH_3), 2.11–2.18 (m, 9H, $3 \times CO_2CH_3$), 2.21–2.27 (m, 6H, CO_2CH_3), 2.44 (s, 3H, CO_2CH_3), 3.75–3.82 (m, 1H, H-6), 3.88 (d, 1H, $J_{2,3}$ 9 Hz, H-2), 3.90 (t, 1H, $J_{5,4} = J_{5,6}$ 10 Hz, H-5), 3.95–4.01 (m, 1H, H-5′), 4.14–4.28 (m, 3H, H-7a, H6′a and H-6′b), 4.56–4.64 (m, 2H, H-2 and H-7b), 5.06 (dd, 1H, $J_{3',4'}$ 3, $J_{3',2'}$ 10.5 Hz, H-3′), 5.14–5.24 (m, 2H, H-4, and H-2′), 5.36 (t, 1H, $J_{3,4} = J_{3,2}$ 8.0 Hz, H-3), 5.25 (d, 1H, $J_{4',3'}$ 3 Hz, H-4′), 9.59–9.63 (m, 1H, H-7); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ (ppm) 20.5, 20.6, 20.7, 21.3 (CH_3CO_2), 60.8 (C-6′), 62.0 (C-7), 66.6 (C-4′), 67.7 (C-4), 69.0 (C-2′), 70.7, 70.8 (C-3′, C-5′), 72.9 (C-3), 75.8 (C-5), 76.4 (C-6), 79.7 (C-2), 101.0 (C-1′), 169.0, 169.6, 169.7, 169.9, 170.0, 170.2 (CH_3CO_2), 195.9 (C-1).

3.11. 5,6,7,9-Tetra-*O*-acetyl-4,8-anhydro-1,3-dideoxy-D-*glycero*-D-*galacto*-non-2-ulose (1e)

A mixture of 4,8-anhydro-1,3-dideoxy-D-*glycero*-D-*galacto*-non-2-ulose[11] (0.31 g, 0.127 mmol) in 2:1 pyridine–Ac_2O (4.5 mL) was stirred for 5 h at rt. After co-evaporation with toluene (3×10 mL), the residue was purified by flash chromatography (13:7→1:1 heptane–EtOAc) to afford the desired compound **1e** as a white solid (0.50 g, 91%). Mp 137–138 °C; $[\alpha]_D^{25}$ −30.5 (*c* 1, $CHCl_3$); ν_{max} (thin film): 1740, 1369, 1219, 1042, 907 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ (ppm) 1.99 (s, 3H, CH_3), 2.05 (s, 3H, CH_3), 2.08 (s, 3H, CH_3), 2.17 (s, 3H, CH_3), 2.20 (s, 3H, CH_3), 2.47 (dd, 1H, $J_{3a,4}$ 4, $J_{3a,3b}$ 17 Hz, H-3a), 2.61 (dd, 1H, $J_{3b,4}$ 9.5, $J_{3b,3a}$ 17 Hz, H-3b), 3.64–3.75 (m, 1H, H-8), 4.05 (d, 1H, $J_{9a,9b}$ 12 Hz, H-9a), 4.16–4.24 (m, 1H, H-4), 4.27 (dd, 1H, $J_{9a,8}$ 5, $J_{9b,9a}$ 12 Hz, H-9b), 5.11 (dd, 1H, $J_{6,5}$ 1, $J_{6,7}$ 10 Hz, H-6), 5.22 (t, 1H, $J_{7,6} = J_{7,8}$ 10 Hz, H-7), 5.32 (d, 1H, $J_{5,6}$ 1 Hz, H-5); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ (ppm) 20.3, 20.5 ($4 \times CO_2CH_3$), 30.4 (C-1), 43.9 (C-3), 62.4 (C-9), 65.8 (C-7), 69.8 (C-5), 71.8 (C-6), 72.6 (C-4), 76.0 (C-8), 169.5, 169.7, 170.2, 170.4 (CO_2CH_3), 204.3 (C-2); ESIMS: $m/z = 411.1$ [$(M+Na)^+$, 100%]; ESIHRMS: m/z 411.1287. $C_{17}H_{24}O_{10}Na_1$ requires 411.1267; Anal. Calcd. for $C_{17}H_{24}O_{10}$: C, 52.57; H, 6.23; O, 41.20. Found: C, 52.72; H, 6.13; O, 41.13.

3.12. 5,6,7,9-Tetra-*O*-acetyl-4,8-anhydro-1-deoxy-D-*erythro*-L-gluco-non-2-ulose and 5,6,7,9-tetra-*O*-acetyl-4,8-anhydro-1-deoxy-D-*erythro*-L-*manno*-non-2-ulose as a mixture (4e) and 5,6,7,9-tetra-*O*-acetyl-4,8-anhydro-3-deoxy-D-*glycero*-D-*galacto*-non-2-ulose (5e)

The enolisation reaction was performed on ketone **1e** (400 mg, 1.03 mmol) according to general procedure A using pyridine (250 μL), TMSCl (390 μL) and then NaI (460 mg) in 6:5 MeCN–cyclohexane (3.8 mL) at 70 °C. After work-up, general procedure B was applied to the crude enol ether **2e** using DMDO (31 mL, 3 equiv) and K_2CO_3 (71 mg). Flash chromatography (7:3→1:1 petroleum ether–EtOAc) gave first **4e** (3:2 mixture of diastereoisomers, 289 mg, 69% from **1e**) followed with **5e** (59 mg, 14%). The major isomer of **4e** can be recrystallised in EtOAc: white solid, mp 163–164 °C; $[\alpha]_D^{25}$ +49.3 (*c* 1, $CHCl_3$); ν_{max} (thin film): 3409, 1722, 1371, 1230, 1102, 1045, 962, 909, 747, 709 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.95 (s, 3H,

CO_2CH_3), 1.99 (s, 3H, CO_2CH_3), 2.05 (s, 3H, CO_2CH_3), 2.10 (s, 3H, CO_2CH_3), 2.36 (s, 3H, C-1), 3.69–3.75 (m, 2H, H-8 and O*H*), 4.05 (dd, 1H, $J_{4,5}$ 1, $J_{4,3}$ 6 Hz, H-4), 4.21 (dd, 1H, $J_{9a,8}$ 2.5, $J_{9a,9b}$ 12 Hz, H-9a), 4.24–4.30 (m, 2H, H-9b, H-3), 5.03 (dd, 1H, $J_{6,5}$ 3, $J_{6,7}$ 10 Hz, H-6), 5.23 (t, 1H, $J_{7,8} = J_{7,6}$ 10 Hz, H-7), 5.54 (dd, 1H, $J_{5,4}$ 1, $J_{5,6}$ 3 Hz, H-5); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 20.1, 20.5, 20.6, 20.7 ($4 \times CO_2CH_3$), 27.4 (C-1), 62.4 (C-9), 65.9 (C-7), 66.0 (C-5), 71.6 (C-6), 74.4 (C-3), 76.8 (C-8), 77.5 (C-4), 169.4, 169.6, 169.9, 170.5 (CO_2CH_3), 207.8 (C-2); ESIMS: $m/z =$ 427 [$(M+Na)^+$, 100%]; ESIHRMS: m/z 427.1211. $C_{17}H_{24}O_{11}Na_1$ requires 427.1211; Anal. Calcd for $C_{17}H_{24}O_{11}$: C, 50.49; H, 5.98; O, 43.52. Found: C, 50.33; H, 5.94; O, 43.31. Compound **5e**: $[\alpha]_D^{25}$ −43.8 (*c* 1, $CHCl_3$); ν_{max} (thin film): 2954, 1737, 1371, 1219, 1044, 962, 906, 734 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.94 (s, 3H, CO_2CH_3), 2.00 (s, 3H, CO_2CH_3), 2.04 (s, 3H, CO_2CH_3), 2.14 (s, 3H, CO_2CH_3), 2.36–2.43 (dd, 1H, $J_{3a,4}$ 4, $J_{3a,3b}$ 16 Hz, H-3a), 2.69–2.77 (dd, 1H, $J_{3b,4}$ 9, $J_{3b,3a}$ 16 Hz, H-3b), 3.65 (ddd, $J_{8,9a}$ 2, $J_{8,9b}$ 6, $J_{8,7}$ 10 Hz, 1H, H-8), 4.03 (dd, 1H, $J_{9a,8}$ 2, $J_{9a,9b}$ 12 Hz, H-9a), 4.17–4.24 (m, 4H, H-4, H-9b, H-1a and H-1b), 5.07 (dd, 1H, $J_{6,5}$ 3, $J_{6,7}$ 10 Hz, H-6), 5.17 (t, 1H, $J_{7,6} = J_{7,8}$ 10 Hz, H-7), 5.31 (d, 1H, $J_{5,6}$ 3 Hz, H-5); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 20.4, 20.6 ($4 \times CO_2CH_3$), 39.5 (C-3), 62.4 (C-9), 65.8 (C-7), 68.8 (C-1), 69.8 (C-5), 71.9 (C-6), 72.6 (C-4), 76.2 (C-8), 169.6, 169.9, 170.4, 170.6 (CO_2CH_3), 206.4 (C-2); ESIMS: $m/z = 427$ [$(M+Na)^+$, 100%]; ESIHRMS: m/z 427.1211. $C_{17}H_{24}O_{11}Na_1$ requires 427.1211.

3.13. Bis(phenylmethyl)imidazolidine of the 3,4,5,7-tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-D-*galacto*-heptose (7e)

Aminal **7e** was then synthesised according to general procedure C. The reaction was performed with crude **4e** (75.6 mg, 0.159 mmol) using $NaIO_4$ (120 mg) for 3 h. After work-up, treatment with *N*,*N*-dibenzylethylenediamine, then flash chromatography (17:3 toluene–EtOAc), **12** (22.7 mg, 27%) closely followed by **7e** (47.6 mg, 51% from **1e**) were obtained. Compound **12**: ν_{max} (ATR-FT IR, diamond prism): 2923, 1741, 1367, 1218, 1048, 909, 741, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.03–2.08 (m, 9H, CO_2CH_3), 2.56–2.62 (m, 2H, N–C*H*2–), 3.04–3.11 (m, 2H, N–C*H*2–), 3.51 (d, 1H, *J* 13 Hz, CH_2-Ph), 3.53 (d, 1H, *J* 13 Hz, CH_2-Ph), 3.60 (s, 1H, H-1), 3.93 (d, 1H, *J* 13 Hz, CH_2-Ph), 3.96 (d, 1H, *J* 13 Hz, CH_2-Ph), 4.21–4.41 (m, 3H, H-6, H-7a and H-7b), 5.10 (d, 1H, $J_{3,4}$ 4 Hz, H-3), 5.19 (dd, 1H, $J_{5,4}$ 4, $J_{5,6}$ 6 Hz, H-5), 5.90 (t, 1H, $J_{4,5} = J_{4,3}$ 4 Hz, H-4), 7.20–7.50 (m, 10H, Ph); ^{13}C NMR (90 MHz, $CDCl_3$): δ (ppm) 20.4, 20.5, 20.8 (CH_3CO_2), 50.4 (CH_2–N), 50.5 (CH_2–N), 57.1 (CH_2-Ph), 59.8 (CH_2-Ph), 61.1 (C-7), 67.0, 67.1 (C-4, C-5), 73.8 (C-6), 84.8 (C-1), 98.1 (C-3), 126.7, 127.1, 128.1, 128.2, 128.3, 128.4, 128.8 (Ph), 138.7 (Cq Ph), 155.0 (C-2), 169.3, 170.0, 170.2 (CO); ESIMS: $m/z = 523$ [$(M+H)^+$, 30%]. Compound **7e**: ν_{max} (thin film): 2944, 1740, 1598, 1434, 1369, 1220, 1041, 910, 742 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.99 (s, 3H, CO_2CH_3), 2.02 (s, 3H, CO_2CH_3), 2.06 (s, 3H, CO_2CH_3), 2.14 (s, 3H, CO_2CH_3), 2.64–2.82 (m, 4H, N–C*H*2–), 3.54–3.60 (m, 3H, CH_2Ph and H-1), 3.68–3.73 (m, 2H, CH_2Ph and H-2), 3.77 (ddd, 1H, $J_{6,7a}$ 2, $J_{6,7b}$ 6, $J_{6,5}$ 9 Hz, H-6), 4.19 (dd, 1H, $J_{7a,6}$ 2, $J_{7a,7b}$ 12 Hz, H-7a), 4.26 (dd, 1H, $J_{7b,6}$ 6, $J_{7a,7b}$ 12 Hz, H-7b), 4.34 (d, 1H, *J* 13 Hz, CH_2Ph), 5.13 (dd, 1H, $J_{4,3}$ 3, $J_{4,5}$ 9 Hz, H-4), 5.29 (t, 1H, $J_{5,4} = J_{5,6}$ 9 Hz, H-5), 5.91 (d, 1H, $J_{3,4}$ 3 Hz, H-3), 7.20–7.50 (m, 10H, Ph); ^{13}C NMR (90 MHz, $CDCl_3$): δ (ppm) 20.6, 20.7, 20.9 (CH_3CO_2), 49.5 (CH_2–N), 49.7 (CH_2–N), 60.4 (CH_2-Ph), 60.7 (CH_2-Ph), 63.3 (C-7), 66.6 (C-5), 69.2 (C-3), 72.7 (C-4), 76.5 (C-6), 81.4 (C-2), 83.6 (C-1), 126.9, 127.2, 128.2, 128.3, 128.7, 130.0 (Ph), 138.7, 138.9 (Cq Ph), 169.8, 170.1, 170.2, 170.8 (CO); ESIMS: $m/z = 605$ [$(M+Na)^+$, 100%]; ESIHRMS: m/z 605.24926. $C_{31}H_{38}O_9N_2Na_1$ requires 605.2470.

3.14. 5-*N*-Acetylacetamido-6,7,9-tri-*O*-acetyl-4,8-anhydro-1,5-dideoxy-D-*erythro*-L-talo-non-2-ulose (4g) and 5-acetamido-6,7,9-tri-*O*-acetyl-4,8-anhydro-1,5-dideoxy-D-*erythro*-L-talo-non-2-ulose (13)

The enolisation reaction was performed on **1g** (0.429 g, 1 mmol) according to general procedure A in 6:5 MeCN–cyclohexane (2.75 mL) using pyridine (0.4 mL), TMSCl (0.64 mL) and NaI (0.74 g) for a night at 70 °C. To this crude residue was added DMDO (30 mL, 0.1 M in acetone, 3 equiv). The soln was stirred for 2 h at rt and concentrated. Flash chromatography (1:1 petroleum ether–EtOAc + 0.1% NEt_3) gave **4g** (0.311 g, 70%): $[\alpha]_D^{20}$ +2.4 (*c* 1, $CHCl_3$); ν_{max} (thin film): 3465, 1749, 1717, 1368, 1226, 1047 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ (ppm) 1.92–2.00 (m, 9H, $3 \times CH_3$), 2.15 (s, 3H, CH_3), 2.29 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 3.69 (ddd, 1H, $J_{8,9a}$ 2.5, $J_{8,9b}$ 6, $J_{8,7}$ 9.5 Hz, H-8), 3.74–3.82 (br s, 1H, OH), 3.91 (dd, 1H, $J_{9a,8}$ 2.5, $J_{9a,9b}$ 13 Hz, H-9a), 3.97–4.06 (m, 2H, H-5 and H-3), 4.08 (dd, 1H, $J_{9b,8}$ 6, $J_{9a,9b}$ 13 Hz, H-9b), 4.92 (dd, 1H, $J_{7,8}$ 9, $J_{7,6}$ 10 Hz, H-7), 5.02 (dd, 1H, $J_{4,3}$ 2.5, $J_{4,5}$ 10 Hz, H-4), 5.76 (dd, 1H, $J_{6,5}$ 9, $J_{6,7}$ 10 Hz, H-6); ^{13}C NMR (90 MHz, $CDCl_3$): δ (ppm) 20.3, 24.6, 24.8, 27.5 (CH_3), 58.0 (C-3), 62.4 (C-9), 69.6 (C-7), 70.9 (C-6), 75.1 (C-5), 76.2 (C-4 and C-8), 169.6, 169.7, 170.4, 174.6, 175.2, ($5 \times CO_2CH_3$), 205.0 (C-2); ESIMS: $m/z = 468$ [$(M+Na)^+$,100%]; Anal. Calcd. for $C_{19}H_{27}O_{11}N$: C, 51.23; H, 6.11; O, 39.51; N, 3.14. Found: C, 50.97; H, 6.12; O, 39.74; N, 2.93. If the oxidation of **1g** is carried out in the presence of K_2CO_3, a substantial amount of **13** is formed. $[\alpha]_D^{20}$ −32.8 (*c* 1, $CHCl_3$); ν_{max} (ATR-FT IR, diamond prism): 2988,

1731, 1651, 1540, 1364, 1219, 1038 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.86 (s, 3H, CH_3), 1.99–2.04 (m, 9H, $3 \times CH_3$), 2.11 (s, 3H, CH_3), 2.24 (s, 3H, CH_3), 3.61 (ddd, 1H, $J_{8,9a}$ 2.5, $J_{8,9b}$ 6, $J_{8,7}$ 9.5 Hz, H-8), 3.87 (dd, 1H, $J_{4,3}$ 2.5, $J_{4,5}$ 10 Hz, H-4), 4.05 (dd, 1H, $J_{9a,8}$ 2.5, $J_{9a,9b}$ 13 Hz, H-9a), 4.17 (dd, 1H, $J_{9b,8}$ 6, $J_{9b,9a}$ 13 Hz, H-9b), 4.37 (q, 1H, $J_{5,4} = J_{5,6} = J_{5,NH}$ 10 Hz, H-5), 4.98 (d, 1H, $J_{4,3}$ 2.5 Hz, H-4), 5.03 (t, 1H, $J_{7,8} = J_{7,6}$ 10 Hz, H-7), 5.08 (t, 1H, $J_{6,5} = J_{6,7}$ 10 Hz, H-6), 5.96 (d, 1H, J 10 Hz, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 20.5, 20.6, 20.7, 22.9, 26.9 (CH_3), 49.2 (C-5), 62.3 (C-9), 68.6 (C-7), 74.0 (C-6), 75.8 (C-3), 76.1 (C-4), 78.7 (C-8), 169.3, 170.0, 170.4, 171.0, 171.3 (CO_2CH_3), 206.3 (C-2); ESIMS: $m/z =$ 468 [$(M+Na)^+$,100%]; ESIHRMS: m/z 468.1486. $C_{19}H_{27}O_{11}N_1Na_1$ requires 468.1476; Anal. Calcd for $C_{19}H_{27}O_{11}N$: C, 51.23; H, 6.11; O, 39.51; N, 3.14. Found: C, 50.94; H, 6.11; O, 39.43; N, 3.03.

3.15. 3-Acetamido-2,6-anhydro-3-deoxy-D-*glycero*-D-*gulo*-heptose (16)

To a soln of aminal **7g** (0.32 mmol, 200 mg) in MeOH (3 mL) was added sodium methoxide (2 mg). After stirring for 1 h at rt, MeOH was evaporated. 1:1 THF–water (3.2 mL) was then added followed with Dowex H^+ resin (400 mg). After stirring for 1 h at rt, the suspension was filtered, concentrated and coevaporated with toluene (3×10 mL).^1H NMR (400 MHz, D_2O): δ (ppm) 2.00 (s, 3H, $COCH_3$), 3.35–3.45 (m, 3H, H-1, H-5 and H-6), 3.50 (t, 1H, $J_{4,3} = J_{4,5}$ 9 Hz, H-4), 3.71 (dd, 1H, $J_{7a,6}$ 4 Hz, $J_{7a,7b}$ 12 Hz, H-7a), 3.73 (t, 1H, $J_{3,4} = J_{3,2}$ 10 Hz, H-3), 3.89 (d, 1H, $J_{7a,7b}$ 12 Hz, H-7b), 4.96 (d, 1H, J 1 Hz, H-1); ^{13}C NMR (100 MHz, D_2O): δ (ppm) 21.8 ($COCH_3$), 51.7 (C-3), 60.8 (C-7), 74.9 (C-4), 69.5, 78.6, 79.1 (C-2, C-5, C-6), 87.5 (C-1), 174.0 ($COCH_3$).

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Supplementary data

Complete crystallographic data for the structural analysis of **4a** have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 646170. Copies of this information may be obtained free of charge from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB21EZ, UK. (fax: +44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk or via: www.ccdc.cam.ac.uk). Typical procedures for the preparation of **6a**,**b**, **6f**,**g**, **10**, **11**, **15** and **17** and their analysis data, ^1H and ^{13}C NMR spectra for **7e** and **12**. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2007.09.002.

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