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Synthesis of methyl 3-amino-3,6-dideoxy-α-D-galactopyranoside carrying different amide substituents†

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Bacterial polysaccharides may contain rare sugars of different stereochemistry and diverse functional groups; the repertoire can be further extended by varying the exocyclic substituents. Synthesis of four monosaccharides is described utilizing a suitably protected key intermediate obtained by regioselective acetal ring-opening reduction, dexoygenation at C6, alcohol oxidation at C3 followed by formation of an oxime, which was stereoselectively reduced by samarium diiodide to give a 3-amino-derivative having the desired *galacto*-configuration. Subsequent functionalization was performed resulting in one to four carbon atoms in the amide substituent.

Introduction

Lipopolysaccharides (LPS) cover a large portion of the outer membrane of Gram-negative bacteria where they play important roles in interactions with host cells.[1] The LPS consists of three parts, namely, the lipid A which anchors it in the membrane, a core region which is the outer part in rough bacteria and the O-antigenic polysaccharide which contains the outer part in smooth type bacteria. Whereas many of the biological effects are the consequences of the interactions of lipid A with the immune system of the host, the O-antigen plays important roles in colonization of the host and resistance to its immune system.

The lipid A and the core region of different bacteria are relatively conserved within a species and usually only a few variants are observed. The O-antigen polysaccharide, on the other hand, shows large variability both with respect to the polymer synthesized and the sugar components being part of it, where to date several hundred different sugar residues have been identified as constituents.[2] Branched sugars with carbon chains extending from the cyclic ring of the monosaccharide[3,4] are rare and many sugars are uncommon only being found in nature in a few instances.[5] The monosaccharide D-Fuc*p*3N (3-amino-3,6-dideoxy-D-galactopyranose) has been found α-linked as a side-chain to the backbone polymer in the O-antigen polysaccharide of *Providencia alcalifaciens* O21 (ref. 6) in which it was *N*-formylated, which also was the case in the O-antigen from *Salmonella enterica* O60.[7] The same type of substitution pattern (terminal side-chain and α-linked) was present in the O-polysaccharide from *Xanthomonas campestris* pv. *campestris* 8004, but here the amino group was *N*-acetylated,[8] which is also the case for the monosaccharide in the glycan chain of the S-layer protein of *Aneurinibacillus thermoaerophilus* L420-91T.[9] In the core part of *Proteus penneri* strain 16 LPS[10] the terminal Fuc3N residue carries an (*R*)-3-hydroxybutyryl group and in the O-antigen from *Pseudoalteromonas nigrifaciens* strain KMM 161 the substituent is a 4-hydroxybutyryl group.[11] In the O-antigens of *Escherichia coli* O74 and *Proteus vulgaris* O45 the D-Fuc*p*3NAc residues are β-linked.[12,13] Herein, we describe the synthesis of methyl 3-amino-3,6-dideoxy-α-D-galactopyranoside having the above four amide-linked groups as substituents.

Results and discussion

The synthesis is described from the monobenzylated 4,6-*O*-benzylidene acetal derivative **5** which previously has been reported in the literature.[14] Benzoylation of the hydroxyl group in position 3 gave the fully protected compound **6** (Scheme 1). The $BH_3 \cdot THF$ complex together with $CoCl_2$ (ref. 15) was used to reductively open the benzylidene acetal in a regioselective fashion[16] to obtain the 6-hydroxy derivative **7**. The use of this reagent was previously shown to result in high selectivity toward producing the 6-hydroxy derivatives in several hexopyranosides and the reaction was also successfully carried out with compound **5** or its 3-*O*-acetyl derivative, but the highest yield (92%) was achieved with the benzoyl derivative **6**.

The deoxygenative reduction of a 6-hydroxyl group was previously shown for an α-D-mannopyranoside derivative by tosylation followed by reduction with sodium borohydride in DMF,[17] but for compound **7** the procedure resulted in the bicyclic 3,6-anhydro product. Instead, bromination with CBr_4 and Ph_3P[18] to give the 6-bromo derivative **8**, followed by reduction with tributyltin hydride in the presence of AIBN[19,20] was successfully used to obtain the 6-deoxy sugar **9**.

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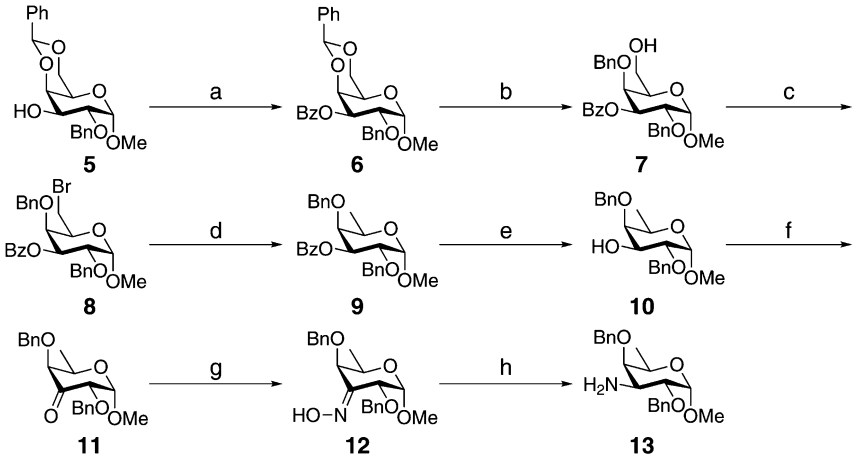
† Electronic supplementary information (ESI) available. ^1H and ^{13}C NMR spectra of all synthesized compounds. See DOI: 10.1039/c3ra45092a



Scheme 1 Synthesis of compounds **6–13**. (a) BzCl, pyridine, 0 °C, 45 min, 93%; (b) BH_3·THF, $CoCl_2$, r.t., 5 h, 92%; (c) Ph_3P, CBr_4, pyridine, 65 °C, 40 min, 99%; (d) Bu_3SnH, AIBN, toluene, 40 min, 81%; (e) MeONa, MeOH, 4 h, 94%; (f) IBX, DMSO, r.t., overnight, 92%; (g) NH_2OH·HCl, NaOAc, EtOH–H_2O, reflux, 2 h, 99%; (h) SmI_2, MeOH, THF, 60 °C, 3 h, 54%.

Deprotection with sodium methoxide in MeOH furnished compound **10**. The oxidation of the L-enantiomer of compound **10** has been reported using 2-iodoxybenzoic acid (IBX) or pyridinium dichromate.[21] The use of IBX[22–24] gave the highest yield (92%) and was thus employed to oxidize **10** to the keto derivative **11**. This was followed by reaction with hydroxylamine hydrochloride[25] to give the oxime **12**.

The key step in the synthesis is the reduction of oxime **12** to the amine derivative **13** having the desired *galacto*-configuration. Different reducing reagents were reported earlier by Hsu *et al.* for the corresponding L-enantiomer,[21] where, for example, Red-Al® favored the *gulo*-configuration, but the highest stereoselectivity for the desired product was achieved by using samarium diiodide[26,27] as a single-electron donor reducing agent (the ratio between *galacto*- and *gulo*-configurations being >19 : 1). This reagent was used to reduce oxime **12** to obtain compound **13** in an isolated yield of 54%. It can be noted that for ethyl 2,4-di-*O*-benzyl-6-deoxy-1-thio-β-D-*xylo*-hexopyranosid-3-ulose (*E*)-oxime reduction with Red-Al® worked well and the amino derivative having the *galacto*-configuration was isolated in 80% yield,[28] highlighting the stereochemical effects of the anomeric configuration on the reduction of the oxime at position 3 of these derivatives.

The target compounds were obtained *via* amide coupling of **13** with activated formic acid[29] and acetic anhydride,[30] respectively, to form compounds **14** and **15**, which were deprotected by catalytic hydrogenolysis over Pd/C to give **1** and **2** (Scheme 2). The acids **16** and **19** were prepared according to Toriizuka *et al.*[31] and Brewer *et al.*,[32] respectively, and were coupled with **13** by using DCC as the coupling reagent[33] to obtain compounds **17** and **20**, respectively. The subsequent deprotection of the silyl ethers was performed with tetra-*n*-butylammonium fluoride (TBAF)[34] in THF to give **18** and **21**, respectively. In the last deprotection step catalytic hydrogenolysis over Pd/C afforded compounds **3** and **4**.

The monosaccharide 3-amino-3,6-dideoxy-α-D-galactopyranose is an unusual component in O-antigen polysaccharides and together with a specific substituent the structure can form a characteristic antigenic determinant, being different (or the same) for the various serogroups in bacteria of diverse origin. The substituents are readily identified by the different ^{1}H chemical shifts (Fig. 1) where the *N*-formyl group in **1** shows two resonances at 8.05 and 8.17 ppm (Fig. 1a) due to two conformations in slow exchange at the amide linkage, a phenomenon observed also for other *N*-formylated sugars.[35,36] The ^{1}H resonance of the *N*-acetyl group in **2** is observed at 2.06 ppm (Fig. 1b). In compound **3** the ^{1}H resonances of the *N*-3-(*R*)-hydroxybutyramido group are present at 1.27, 2.51 and 4.25 ppm (Fig. 1c) whereas in compound **4** having an *N*-4-hydroxybutyramido group they are instead found at 1.86, 2.39 and 3.62 ppm (Fig. 1d), clearly differing between the compounds.

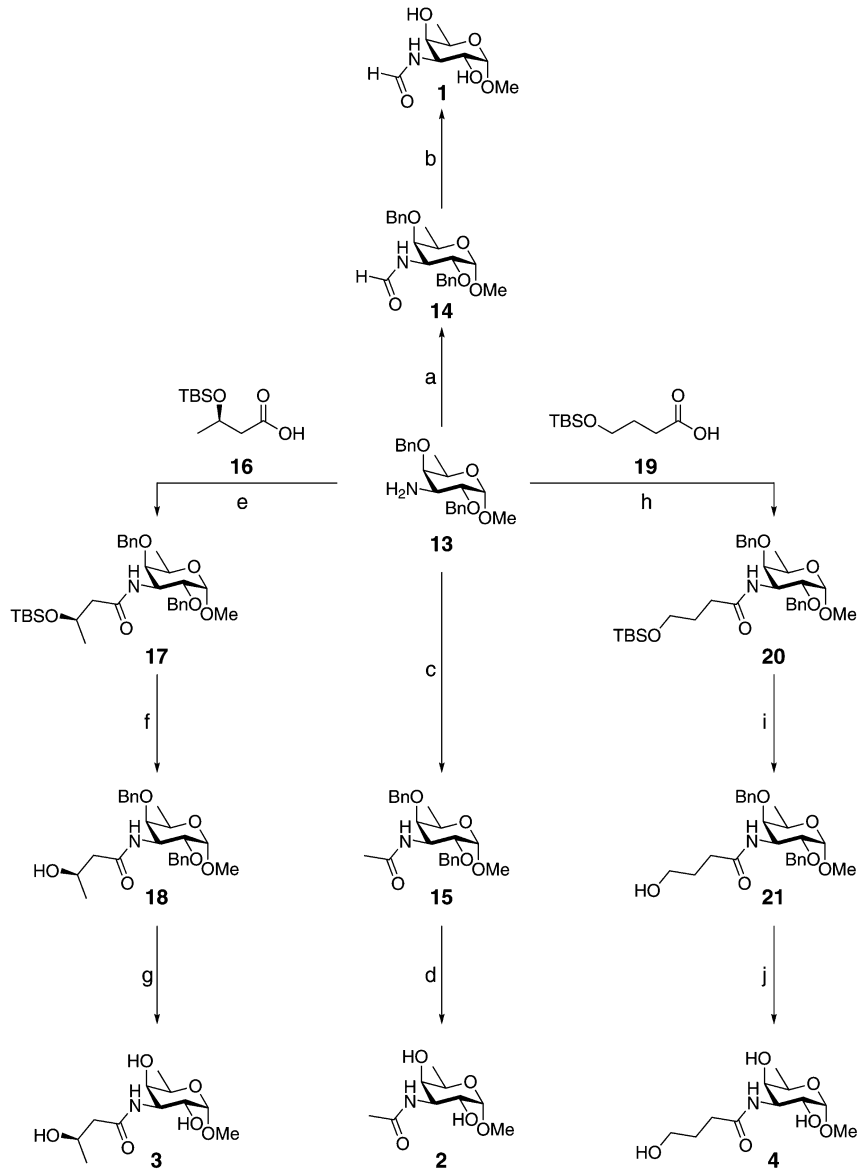
Conclusions

The synthesis has produced four variants with differently attached amide substituents on methyl 3-amino-3,6-dideoxy-α-D-galactopyranoside. The synthesis methodology applied herein will be of use in formation of larger oligosaccharides containing 3-amino-3,6-dideoxy-α-D-galactopyranoside as a component and the ^{1}H and ^{13}C NMR data obtained can be utilized to improve the NMR chemical shift predictions of oligo- and polysaccharides.[37,38]

Experimental section

General experimental methods

All reagents were used as delivered. Column chromatography was performed manually on silica gel with a pore size of 60 Å or by using a Biotage Isolera flash purification system with KP-Sil snap chromatography cartridges. TLC was carried out on silica gel 60 F254 (20 × 20 cm, 0.2 mm thickness), and monitored with either UV light 254 nm, sulfuric acid 8%, Cerium molybdate or $KMnO_4$. NMR spectra were recorded at 25 °C, except for compounds **1–4** which were recorded at 15 °C, on spectrometers operating at a ^{1}H



Scheme 2 Synthesis of compounds **14–21** and **1–4** (a) HCO_2H–Ac_2O, r.t., 24 h, 99%; (b) H_2, Pd/C, EtOH–EtOAc, 4 h, 88%; (c) Ac_2O, EtOAc, r.t., overnight, 82%; (d) H_2, Pd/C, EtOH–EtOAc, 4 h, 75%; (e) DCC, DMAP, DCM, r.t., 3 h, 90%; (f) TBAF, THF, r.t., 30 min, 97%; (g) H_2, Pd/C, EtOH–EtOAc, 4 h, 60%; (h) DCC, DMAP, DCM, r.t., 3 h, 89%; (i) TBAF, THF, r.t., 1 h, 70%; (j) H_2, Pd/C, EtOH, 4 h, 74%.

frequency of 400 or 500 MHz. The NMR chemical shifts are reported in ppm and for ^{1}H referenced to TMS, sodium 3-trimethylsilyl-(2,2,3,3-$^2H_4$)-propanoate (TSP), both set to 0 ppm, or the residual $CHCl_3$ solvent peak at 7.26 ppm as an internal standard; for ^{13}C the chemical shifts were referenced to 1,4-dioxane in D_2O, 67.40 ppm, using an external standard or internally to the $CDCl_3$ solvent signal at 77.16 ppm. For compounds **1–4** ^{1}H chemical shifts and J_{HH} coupling constants were refined from 1D ^{1}H NMR spectra using NMR spin simulation methodology.[39] Mass spectra were recorded on a Bruker Daltonics micrOTOF spectrometer in the positive mode.

Methyl 3-*O*-benzoyl-2-*O*-benzyl-4,6-*O*-benzylidene-α-D-galactopyranoside (6). Compound **5** (4.01 g, 10.80 mmol) was dissolved in pyridine whereafter BzCl (1.38 mL, 11.87 mmol) was added at 0 °C and the solution was stirred for 40 min. The pyridine was evaporated under reduced pressure and the crude material was filtered through a silica gel plug to obtain the product as a white solid (4.80 g, 10.07 mmol, 93%). ^{1}H NMR ($CDCl_3$): δ 3.44 (s, 3 H, OMe), 3.80 (m, 1H, H-5), 4.08 (dd, $J_{H5,H6a}$ 1.70 Hz, J_{gem} 12.53, 1H, H-6a), 4.25 (dd, $J_{H1,H2}$ 3.49 Hz, $J_{H2,H3}$ 10.49 Hz, 1 H, H-2), 4.27 (dd, $J_{H5,H6b}$ 1.70 Hz, J_{gem} 12.53 Hz, 1H, H-6b), 4.58 (dd, $J_{H3,H4}$ 3.57 Hz, $J_{H4,H5}$ 1.32 Hz, 1H, H-4), 4.65 (d, J_{gem} 12.22 Hz, 1H, $PhCH_2$), 4.76 (d, J_{gem} 12.22 Hz, 1H, $PhCH_2$), 4.87 (d, $J_{H1,H2}$ 3.49 Hz, 1H, H-1), 5.51 (s, 1H, PhCH), 5.57 (dd, $J_{H2,H3}$ 10.49 Hz, $J_{H3,H4}$ 3.57 Hz, 1H, H-3), 7.23–8.07 (m, 15 H, H–Ar). ^{13}C NMR ($CDCl_3$): δ 55.8 (OMe), 62.3 (C-5), 69.4 (C-6), 71.4 (C-3), 73.6 ($PhCH_2$), 73.8 (C-2), 74.5 (C-4), 99.4 (C-1), 100.6 (PhCH), 126.2–133.2 (16 C–Ar), 137.9, 138.2 (2 × C-*ipso*), 166.3 (CO). ESIMS: $[M + Na]^+$ *m*/*z* calcd for $C_{28}H_{28}O_7Na$ 499.1727, found 499.1730.

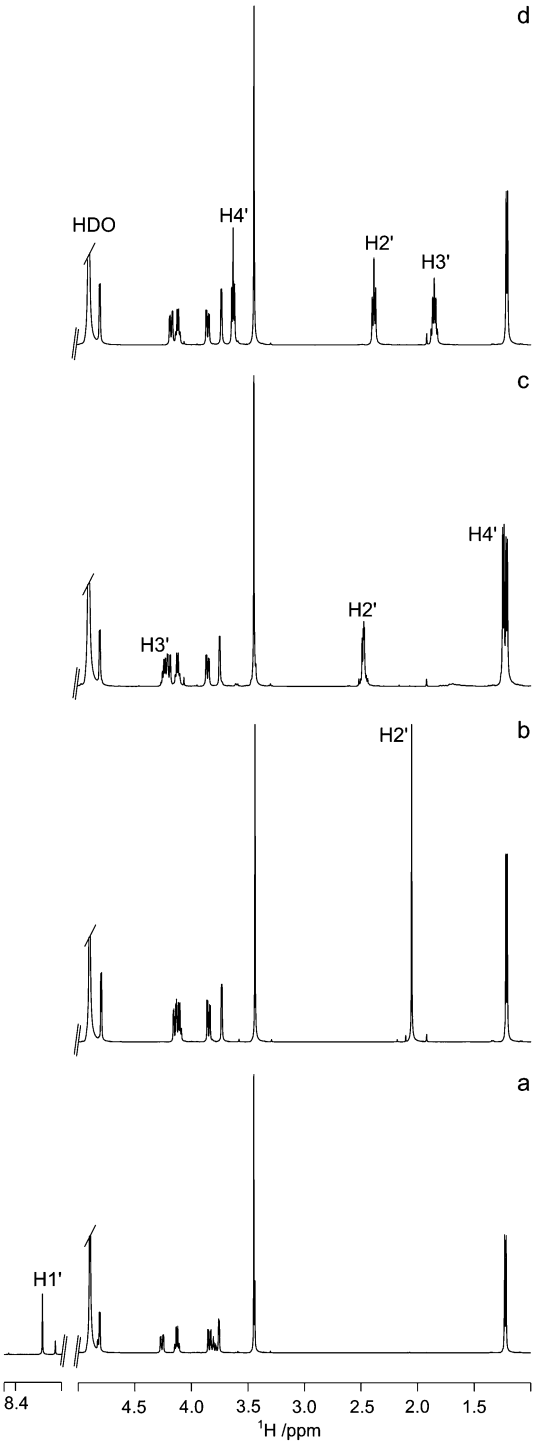


Fig. 1 ^{1}H NMR spectra of compounds **1–4** (a–d) together with annotation of the resonances from their amide substituents.

Methyl 3-*O*-benzoyl-2,4-di-*O*-benzyl-α-D-galactopyranoside (7). Compound **6** (3.80 g, 8.00 mmol) was dissolved in $BH_3 \cdot THF$ complex 1.0 M solution (120.0 mL, 120.0 mmol) followed by the addition of $CoCl_2$ (3.10 g, 24.00 mmol), and the reaction was stirred at r.t. for 5 h. The reaction was diluted with EtOAc and aqueous $NaBH_4$ (0.20 equivalent) was added, and stirred for a few min followed by washing with $NaHCO_3$, water and brine. The solvent was evaporated and the crude mixture was chromatographed over silica gel (toluene–EtOAc 1 : 1) to afford the product as a colorless syrup (3.52 g, 7.35 mmol, 92%). ^{1}H NMR ($CDCl_3$): δ 1.67 (distorted m, 1H, OH), 3.41 (s, 3 H, OMe), 3.55 (distorted m, 1H, H-6a), 3.76 (dd, $J_{H5,H6b}$ 6.76 Hz, J_{gem} 11.35 Hz, 1H, H-6b), 3.95 (m, 1H, H-5), 4.14 (dd, $J_{H3,H4}$ 3.10 Hz, $J_{H4,H5}$ 1.43 Hz, 1H, H-4), 4.20 (dd, $J_{H1,H2}$ 3.61 Hz, $J_{H2,H3}$ 10.54 Hz, 1H, H-2), 4.46 (d, J_{gem} 11.80 Hz, 1H, $PhCH_2$), 4.66 (d, J_{gem} 12.35 Hz, 1H, $PhCH_2$), 4.72 (d, J_{gem} 12.35 Hz, 1H, $PhCH_2$), 4.72 (d, J_{gem} 11.80 Hz, 1H, $PhCH_2$), 4.82 (d, $J_{H1,H2}$ 3.61 Hz, 1H, H-1), 5.56 (dd, $J_{H2,H3}$ 10.54 Hz, $J_{H3,H4}$ 3.10 Hz, 1H, H-3), 7.20–8.04 (m, 15H, H–Ar). ^{13}C NMR ($CDCl_3$): δ 55.6 (OMe), 62.3 (C-6), 70.1 (C-5), 73.3 (C-3), 73.3 ($PhCH_2$), 74.2 (C-2), 75.1 ($PhCH_2$), 75.5 (C-4), 98.7 (C-1), 128.0–133.4 (16 C–Ar), 137.6, 138.2 (2 × C-*ipso*), 166.0 (CO). ESIMS: $[M + Na]^+$ *m*/*z* calcd for $C_{28}H_{30}O_7Na$ 501.1884, found 501.1880.

Methyl 3-*O*-benzoyl-2,4-di-*O*-benzyl-6-bromo-α-D-galactopyranoside (8). To a solution of compound **7** (0.89 g, 1.70 mmol) in pyridine, PPh_3 (0.89 g, 3.40 mmol) and CBr_4 (0.62 g, 1.87 mmol) were added and stirred at 65 °C for 40 min. The mixture was cooled, diluted with MeOH and stirred for 5 min, whereafter it was concentrated and purified by column chromatography (pentane–EtOAc 5 : 1) to give the product as white crystals (0.93 g, 1.69 mmol, 99%). ^{1}H NMR ($CDCl_3$): δ 3.33 (dd, $J_{H5,H6a}$ 6.90 Hz, J_{gem} 10.20 Hz, 1H, H-6a), 3.41 (dd, $J_{H5,H6b}$ 6.90 Hz, J_{gem} 10.20 Hz, 1H, H-6b), 3.44 (s, 3H, OMe), 4.08 (m, 1H, H-5), 4.17 (dd, $J_{H1,H2}$ 3.60 Hz, $J_{H2,H3}$ 10.53 Hz, 1H, H-2), 4.27 (dd, $J_{H3,H4}$ 3.10 Hz, $J_{H4,H5}$ 1.42 Hz, 1H, H-4), 4.52 (d, J_{gem} 11.30, 1H, $PhCH_2$), 4.64 (d, J_{gem} 12.31 Hz, 1H, $PhCH_2$), 4.71 (d, J_{gem} 12.31 Hz, 1H, $PhCH_2$), 4.75 (d, J_{gem} 11.30 Hz, 1H, $PhCH_2$), 4.77 (d, $J_{H1,H2}$ 3.60 Hz, 1H, H-1), 5.58 (dd, $J_{H2,H3}$ 10.53 Hz, $J_{H3,H4}$ 3.10 Hz, 1H, H-3), 7.22–8.04 (m, 15H, H–Ar). ^{13}C NMR ($CDCl_3$): δ 30.1 (C-6), 55.8 (OMe), 70.5 (C-5), 73.2 (C-3), 73.4 ($PhCH_2$), 73.9 (C-2), 75.6 ($PhCH_2$), 75.6 (C-4), 98.8 (C-1), 128.0–133.4 (16 C–Ar), 137.7, 138.1 (2 × C-*ipso*), 165.9 (CO). ESIMS: $[M + Na]^+$ *m*/*z* calcd for $C_{28}H_{29}BrO_6Na$ 563.1040, found 563.1028.

Methyl 3-*O*-benzoyl-2,4-di-*O*-benzyl-6-deoxy-α-D-galactopyranoside (9). Bu_3SnH (9.84 mL, 36.60 mmol) and compound **8** (3.30 g, 6.10 mmol) were dissolved in toluene, stirred for 5 min at 95 °C, followed by the addition of AIBN (0.36 g, 2.20 mmol) and the stirring continued for 40 min at the same temperature. The solvent was evaporated under reduced pressure and the crude mixture was purified by column chromatography over silica gel (pentane–EtOAc 5 : 1) to obtain the product as a colorless syrup (2.29 g, 4.95 mmol, 81%). ^{1}H NMR ($CDCl_3$): δ 1.17 (d, $J_{H5,H6}$ 6.56 Hz, 3H, Me-6), 3.40 (s, 3H, OMe), 3.90 (dd, $J_{H3,H4}$ 3.13 Hz, $J_{H4,H5}$ 1.31 Hz, 1H, H-4), 4.05 (m, 1H, H-5), 4.17 (dd, $J_{H2,H3}$ 10.53 Hz, $J_{H1,H2}$ 3.64 Hz, 1H, H-2), 4.51 (d, J_{gem} 11.47 Hz, 1H, $PhCH_2$), 4.65 (d, J_{gem} 12.35 Hz, 1H, $PhCH_2$), 4.68 (d, J_{gem} 11.47 Hz, 1H, $PhCH_2$), 4.70 (d, J_{gem} 12.35 Hz, 1H, $PhCH_2$), 4.76 (d, $J_{H1,H2}$ 3.64 Hz, 1H, H-1), 5.54 (dd, $J_{H2,H3}$ 10.53 Hz, $J_{H3,H4}$ 3.13 Hz, 1H, H-3), 7.21–8.02 (m, 15H, H–Ar). ^{13}C NMR ($CDCl_3$): δ 16.5 (C-6), 55.5 (OMe), 65.9 (C-5), 73.3 (C-3), 73.7 ($PhCH_2$), 74.0 (C-2), 75.6 ($PhCH_2$), 78.3 (C-4), 98.7 (C-1), 127.7–133.3 (16 C–Ar), 138.0, 138.3 (2 × C-*ipso*), 166.1 (CO). ESIMS: $[M + Na]^+$ *m*/*z* calcd for $C_{28}H_{30}O_6Na$ 485.1935, found 485.1922.

Methyl 2,4-di-*O*-benzyl-6-deoxy-α-D-galactopyranoside (10). To a solution of compound **9** (2.20 g, 4.75 mmol) in MeOH, 1 M

NaOMe in MeOH was added dropwise until pH 8 and stirred for 4 h. The reaction was quenched with Dowex 50 H^+, filtered and chromatographed over silica gel (pentane–EtOAc 1 : 1) to obtain the product as a white solid (1.60 g, 4.46 mmol, 94%). ^{1}H NMR ($CDCl_3$): δ 1.18 (d, $J_{H5,H6}$ 6.60 Hz, 3H, Me-6), 2.24 (d, $J_{H3,OH}$ 4.75 Hz, 1H, OH), 3.32 (s, 3H, OMe), 3.64 (dd, $J_{H3,H4}$ 3.33 Hz, $J_{H4,H5}$ 1.30 Hz, 1H, H-4), 3.78 (dd, $J_{H1,H2}$ 3.49 Hz, $J_{H2,H3}$ 10.06 Hz, 1H, H-2), 3.89 (m, 1H, H-5), 4.06 (ddd, $J_{H2,H3}$ 10.06 Hz, $J_{H3,OH}$ 4.75 Hz, $J_{H3,H4}$ 3.33 Hz, 1H, H-3), 4.65 (d, J_{gem} 12.33 Hz, 1H, $PhCH_2$), 4.66 (d, $J_{H1,H2}$ 3.49 Hz, 1H, H-1), 4.70 (d, J_{gem} 12.33 Hz, 1H, $PhCH_2$), 4.70 (d, J_{gem} 11.66 Hz, 1H, $PhCH_2$), 4.84 (d, J_{gem} 11.66 Hz, 1H, $PhCH_2$), 7.27–7.40 (m, 10H, H–Ar). ^{13}C NMR ($CDCl_3$): δ 16.8 (C-6), 55.5 (OMe), 66.1 (C-5), 70.7 (C-3), 73.0 ($PhCH_2$), 75.6 ($PhCH_2$), 77.3 (C-2), 79.6 (C-4), 98.1 (C-1), 127.9–128.6 (10 C–Ar), 138.3, 138.6 (2 × C-*ipso*). ESIMS: $[M + Na]^+$ *m*/*z* calcd for $C_{21}H_{26}O_5Na$ 381.1672, found 381.1682.

Methyl 2,4-di-*O*-benzyl-6-deoxy-3-oxo-α-D-*xylo*-pyranoside (11). Compound **10** (0.35 g, 0.97 mmol) and prepared *o*-iodoxybenzoic acid[23] (2.70 g, 9.65 mmol) were dissolved in DMSO (15 mL) and stirred at r.t. overnight. The reaction mixture was diluted with water and extracted with DCM. The organic layer was washed with water, dried with sodium sulfate and concentrated, followed by column chromatography over silica gel (pentane–EtOAc, 3 : 1) to obtain the product as a colorless syrup (0.32 g, 0.90 mmol, 92%). ^{1}H NMR ($CDCl_3$): δ 1.28 (d, $J_{H5,H6}$ 6.52 Hz, 3H, Me-6), 3.36 (s, 3H, OMe), 3.60 (d, $J_{H4,H5}$ 1.70 Hz, 1H, H-4), 4.10 (m, 1H, H-5), 4.30 (d, J_{gem} 11.84 Hz, 1H, $PhCH_2$), 4.46 (d, J_{gem} 11.84 Hz, 1H, $PhCH_2$), 4.51 (d, J_{gem} 12.33 Hz, 1H, $PhCH_2$), 4.64 (d, $J_{H1,H2}$ 4.20 Hz, 1H, H-2), 4.80 (d, J_{gem} 12.33 Hz, 1H, $PhCH_2$), 4.96 (d, $J_{H1,H2}$ 4.20 Hz, 1H, H-1), 7.24–7.30 (m, 10H, H–Ar).^{13}C NMR ($CDCl_3$): δ 15.5 (C-6), 55.6 (OMe), 68.4 (C-5), 72.2 ($PhCH_2$), 72.7 ($PhCH_2$), 78.7 (C-2), 84.4 (C-4), 101.6 (C-1), 128.3–128.6 (10 C–Ar), 136.7, 137.1 (2 × C-*ipso*), 203.7 (CO). ESIMS: $[M + Na]^+$ *m*/*z* calcd for $C_{21}H_{24}O_5Na$ 379.1516, found 379.1520.

Methyl 2,4-di-*O*-benzyl-3,6-dideoxy-3-hydroxyimino-α-D-*xylo*-pyranoside (12). Compound **11** (1.10 g, 3.08 mmol), $NH_2OH \cdot HCl$ (0.32 g, 4.63 mmol) and NaOAc (0.63 g, 7.72 mmol) were dissolved in water–EtOH 3 : 1 (28 mL) and refluxed for 4 h. The mixture was cooled, filtrated and the precipitate was washed with water to obtain the product as colorless needles (1.14 g, 3.07 mmol, 99%). ^{1}H NMR ($CDCl_3$): δ 1.23 (d, $J_{H5,H6}$ 6.57 Hz, 3H, Me-6), 3.37 (s, 3H, OMe), 3.96 (m, 1H, H-5), 4.38 (d, J_{gem} 12.02 Hz, 1H, $PhCH_2$), 4.52 (d, $J_{H1,H2}$ 3.63 Hz, 1H, H-2), 4.56 (d, J_{gem} 12.02 Hz, 1H, $PhCH_2$), 4.58 (d, J_{gem} 12.44 Hz, 1H, $PhCH_2$), 4.78 (d, $J_{H1,H2}$ 3.63 Hz, 1H, H-1), 4.83 (d, $J_{H4,H5}$ 1.68 Hz, 1H, H-4), 4.83 (d, J_{gem} 12.44 Hz, 1H, $PhCH_2$), 7.27–7.38 (m, 10H, H–Ar).^{13}C NMR ($CDCl_3$): δ 16.0 (C-6), 55.5 (OMe), 66.9 (C-5), 70.0 (C-4), 71.4 ($PhCH_2$), 72.5 ($PhCH_2$), 73.1 (C-2), 99.8 (C-1), 127.9–128.6 (10 C–Ar), 137.7, 137.8 (2 × C-*ipso*), 152.9 (C-3). ESIMS: $[M + Na]^+$ *m*/*z* calcd for $C_{21}H_{25}NO_5Na$ 394.1625, found 394.1634.

Methyl 3-amino-2,4-di-*O*-benzyl-3,6-dideoxy-α-D-galactopyranoside (13). Compound **12** (0.20 g, 0.54 mmol) was dissolved in a small amount of THF, samarium diiodide (0.1 M in THF, 80 mL, 8.0 mmol) and MeOH (0.14 mL, 3.5 mmol) were added and stirred at 60 °C for 3 h. The reaction was quenched with saturated solution of $Na_2S_2O_3$ and $NaHCO_3$ 1 : 1 (40 mL) and extracted with DCM. The organic layer was washed with water, dried over sodium sulfate, concentrated and chromatographed over silica gel (pentane–acetone 1 : 3) to obtain **13** as a pale yellow syrup (0.10 g, 0.29 mmol, 54%). ^{1}H NMR ($CDCl_3$): δ 1.22 (d, $J_{H5,H6}$ 6.66 Hz, 3H, Me-6), 3.12 (dd, $J_{H2,H3}$ 10.40 Hz, $J_{H3,H4}$ 3.15 Hz, 1H, H-3), 3.35 (s, 3H, OMe), 3.49 (dd, $J_{H2,H3}$ 10.40 Hz, $J_{H1,H2}$ 3.42 Hz, 1H, H-2), 3.61 (d, $J_{H3,H4}$ 3.15 Hz, 1H, H-4), 3.94 (m, 1H, H-5), 4.56 (d, J_{gem} 11.82 Hz, 1H, $PhCH_2$), 4.64 (d, J_{gem} 11.82 Hz, 1H, $PhCH_2$), 4.67 (d, J_{gem} 11.30 Hz, 1H, $PhCH_2$), 4.69 (d, $J_{H1,H2}$ 3.42 Hz, 1H, H-1), 4.72 (d, J_{gem} 11.30 Hz, 1H, $PhCH_2$), 7.28–7.35 (m, 10H, H–Ar). ^{13}C NMR ($CDCl_3$): δ 16.9 (C-6), 51.8 (C-3), 55.4 (OMe), 66.9 (C-5), 72.7 ($PhCH_2$), 76.4 ($PhCH_2$), 78.7 (C-2), 81.6 (C-4), 97.6 (C-1), 127.9–128.6 (10 C–Ar), 138.3, 138.4 (2 × C-*ipso*). ESIMS: $[M + Na]^+$ *m*/*z* calcd for $C_{21}H_{27}NO_4Na$ 380.1832, found 380.1820.

Methyl 2,4-di-*O*-benzyl-3-formamido-3,6-dideoxy-α-D-galactopyranoside (14). Acetic anhydride (10 mL) and formic acid (4.70 mL) were heated at 60 °C for 4 h, then 2 mL were added to compound **13** (30 mg, 0.08 mmol) and the mixture was stirred at r.t. for 24 h. The solvent was evaporated and the crude was purified by column chromatography (pentane–acetone 3 : 1) to obtain the product as white solid (32 mg, 0.08 mmol, 99%). Major ^{1}H NMR ($CDCl_3$): δ 1.21 (d, $J_{H5,H6}$ 6.62 Hz, 1.8H, Me-6), 3.38 (s, 1.8H, OMe), 3.70 (dd, $J_{H1,H2}$ 3.36 Hz, $J_{H2,H3}$ 11.20 Hz, 0.6H, H-2), 4.41 (d, J_{gem} 11.90 Hz, 0.6H, $PhCH_2$), 4.42 (m, 0.6H, H-3), 4.47 (d, J_{gem} 12.15 Hz, 0.6H, $PhCH_2$), 4.65 (d, J_{gem} 12.15 Hz, 0.6H, $PhCH_2$), 4.73 (d, J_{gem} 11.90 Hz, 0.6H, $PhCH_2$), 4.77 (d, $J_{H1,H2}$ 3.36 Hz, 0.6H, H-1), 5.10 (d, $J_{H3,NH}$ 7.30 Hz, 0.6H, NH), 7.24–7.41 (m, 6H, 10 H–Ar), 7.75 (dd, *J* 0.93 Hz, 1.70 Hz, 0.6H, HCO). ^{13}C NMR ($CDCl_3$): δ 16.6 (C-6), 48.6 (C-3), 55.4 (OMe), 65.9 (C-5), 72.2 ($PhCH_2$), 73.8 (C-2), 76.2 ($PhCH_2$), 79.6 (C-4), 97.5 (C-1), 128.0–128.9 (5 C–Ar), 138.0, 138.2 (2 × C-*ipso*), 161.0 (CO). Minor ^{1}H NMR ($CDCl_3$): 1.27 (d, $J_{H5,H6}$ 6.70 Hz, 1.2H, Me-6), 3.37 (s, 1.2H, OMe), 3.54 (dd, $J_{H2,H3}$ 10.41 Hz, $J_{H1,H2}$ 3.50 Hz, 0.4H, H-2), 3.59 (dd, $J_{H3,H4}$ 3.40 Hz, $J_{H4,H5}$ 1.24 Hz, 0.4H, H-4), 3.74 (dd, $J_{H3,H4}$ 3.22 Hz, $J_{H4,H5}$ 1.23 Hz, 0.6H, H-4), 3.80 (ddd, $J_{H2,H3}$ 10.41 Hz, $J_{H3,NH}$ 10.72 Hz, $J_{H3,H4}$ 3.40 Hz, 0.4H, H-3), 3.98 (m, 1H, H-5, H-5), 4.51 (d, J_{gem} 11.90 Hz, 0.4H, $PhCH_2$), 4.55 (d, J_{gem} 11.33 Hz, 0.4H, $PhCH_2$), 4.61 (d, J_{gem} 11.90 Hz, 0.4H, $PhCH_2$), 4.65 (d, $J_{H1,H2}$ 3.50 Hz, 0.4H, H-1), 4.76 (d, J_{gem} 11.33 Hz, 0.4H, $PhCH_2$), 5.55 (dd, $J_{H3,NH}$ 10.72 Hz, $J_{NH,HCO}$ 11.85, 0.4H, NH), 7.24–7.41 (m, 4H, 10 H–Ar), 8.12 (d, $J_{NH,HCO}$ 11.85 Hz, 0.4H, HCO). ^{13}C NMR ($CDCl_3$): δ 16.9 (C-6), 52.4 (C-3), 55.5 (OMe), 66.1 (C-5), 73.3 ($PhCH_2$), 74.7 (C-2), 76.5 ($PhCH_2$), 80.6 (C-4), 97.6 (C-1), 128.0–128.9 (5 C–Ar), 137.2, 137.6 (2 × C-*ipso*), 164.5 (CO). ESIMS: $[M + Na]^+$ *m*/*z* calcd for $C_{22}H_{27}NO_5Na$ 408.1781, found 408.1777.

Methyl 3-formamido-3,6-dideoxy-α-D-galactopyranoside (1). Compound **14** (32 mg, 0.08 mmol) was dissolved in 4 mL EtOAc–EtOH 1 : 1, a catalytic amount of 20% Pd/C was added and **14** was hydrogenolyzed at 100 psi for 4 h. The reaction mixture was filtered through Celite and the solvent was evaporated to afford the product as a white solid (15 mg, 0.07 mmol, 88%). Major ^{1}H NMR (D_2O): δ 1.22 (d, $J_{H5,H6}$ 6.58 Hz, 2.4H, Me-6), 3.45 (2.4H, OMe), 3.76 (dd, $J_{H3,H4}$ 3.15 Hz, $J_{H4,H5}$ 1.34 Hz, 0.8H, H-4), 3.84 (dd, $J_{H2,H3}$ 11.08 Hz, $J_{H1,H2}$ 3.80 Hz, 0.8H, H-2), 4.12 (dd, $J_{H4,H5}$ 1.34 Hz, $J_{H5,H6}$ 6.58 Hz, 0.8H H-5), 4.26 (ddd, $J_{H2,H3}$ 11.08 Hz,

$J_{H3,H4}$ 3.15 Hz, $J_{H3,HCO}$ 0.58 Hz, 0.8H, H-3), 4.81 (d, $J_{H1,H2}$ 3.80 Hz, 0.8H, H-1), 8.17 (d, $J_{H3,HCO}$ 0.58 Hz, 0.8H, HCO). ^{13}C NMR (D_2O): 16.0 (C-6), 50.7 (C-3), 55.9 (OMe), 66.7 (C-2), 67.2 (C-5), 71.0 (C-4), 99.7 (C-1), 165.1 (CO). Minor ^{1}H NMR (D_2O): δ 1.22 (d, $J_{H5,H6}$ 6.53 Hz, 0.6H, Me-6), 3.44 (0.6H, OMe), 3.78 (dd, $J_{H3,H4}$ 3.42 Hz, $J_{H4,H5}$ 1.00 Hz, 0.2H, H-4), 3.80 (dd, $J_{H1,H2}$ 4.45 Hz, $J_{H2,H3}$ 11.03 Hz, 0.2H, H-2), 3.81 (dd, $J_{H2,H3}$ 11.03 Hz, $J_{H3,H4}$ 3.42 Hz, 0.2H, H-3), 4.12 (dd, $J_{H4,H5}$ 1.00 Hz, $J_{H5,H6}$ 6.53 Hz, 0.2H, H-5), 4.83 (d, $J_{H1,H2}$ 4.45 Hz, 0.2H, H-1), 8.05 (s, 0.2H, HCO). ^{13}C NMR (D_2O): δ 15.9 (C-6), 55.2 (C-3), 55.8 (OMe), 66.6 (C-2), 67.4 (C-5), 72.0 (C-4), 99.7 (C-1), 168.2 (CO). ESIMS: $[M + Na]^+$ m/z calcd for $C_8H_{15}NO_5Na$ 228.0842, found 228.0852.

Methyl 3-acetamido-2,4-di-*O*-benzyl-3,6-dideoxy-α-D-galactopyranoside (15). Compound **13** (23 mg, 0.064 mmol) was dissolved in EtOAc (2 mL), acetic anhydride (7.5 mg, 0.073 mmol) was added and the mixture was stirred at r.t. overnight. The reaction mixture was filtered through Celite and the solvent was evaporated under reduced pressure to give the product as a white solid (21 mg, 0.053 mmol, 82%). ^{1}H NMR ($CDCl_3$): δ 1.22 (d, $J_{H5,H6}$ 6.61 Hz, 3H, Me-6), 1.56 (s, 3H, NAc), 3.39 (s, 3H, OMe), 3.69 (dd, $J_{H2,H3}$ 10.90 Hz, $J_{H1,H2}$ 3.31 Hz, 1H, H-2), 3.76 (dd, $J_{H3,H4}$ 3.18 Hz, $J_{H4,H5}$ 1.31 Hz, 1H, H-4), 3.99 (m, 1H, H-5), 4.32 (ddd, $J_{H2,H3}$ 10.90 Hz, $J_{H3,NH}$ 7.44 Hz, $J_{H3,H4}$ 3.18 Hz, 1H, H-3), 4.35 (d, J_{gem} 12.07 Hz, 1H, $PhCH_2$), 4.44 (d, J_{gem} 12.33 Hz, 1H, $PhCH_2$), 4.68 (d, J_{gem} 12.33 Hz, 1H, $PhCH_2$), 4.73 (d, J_{gem} 12.07 Hz, 1H, $PhCH_2$), 4.80 (d, $J_{H1,H2}$ 3.31 Hz, 1H, H-1), 4.96 (d, $J_{H3,NH}$ 7.44 Hz, 1H, NH), 7.21–7.36 (m, 10H, H–Ar). ^{13}C NMR ($CDCl_3$): δ 16.7 (C-6), 23.2 (NAc), 49.8 (C-3), 55.4 (OMe), 66.0 (C-5), 72.2 ($PhCH_2$), 73.8 (C-2), 76.4 ($PhCH_2$), 80.1 (C-4), 97.6 (C-1), 128.1–128.7 (10 C–Ar), 138.3, 138.5 (2 × C-*ipso*), 170.0 (CO). ESIMS: $[M + Na]^+$ m/z calcd for $C_{23}H_{29}NO_5Na$ 422.1938, found 422.1932.

Methyl 3-acetamido-3,6-dideoxy-α-D-galactopyranoside (2). Compound **15** (21 mg, 0.053 mmol) was dissolved in 4 mL EtOAc–EtOH 1 : 1, and deprotected as for compound **14** to obtain the product as a white solid (8.7 mg, 0.039 mmol, 75%). ^{1}H NMR (D_2O): δ 1.22 (d, $J_{H5,H6}$ 6.56 Hz, 3H, Me-6), 2.05 (s, 3H, NAc), 3.44 (s, 3H, OMe), 3.73 (dd, $J_{H3,H4}$ 3.10 Hz, $J_{H4,H5}$ 1.19 Hz, 1H, H-4), 3.85 (dd, $J_{H2,H3}$ 11.14 Hz, $J_{H1,H2}$ 3.82 Hz, 1H, H-2), 4.10 (dd, $J_{H4,H5}$ 1.19 Hz, $J_{H5,H6}$ 6.56 Hz, 1H, H-5), 4.15 (dd, $J_{H2,H3}$ 11.14 Hz, $J_{H3,H4}$ 3.10 Hz, 1H, H-3), 4.80 (d, $J_{H1,H2}$ 3.82 Hz, 1H, H-1), ^{13}C NMR (D_2O): δ 16.0 (C-6), 22.7 (NAc), 52.1 (C-3), 55.9 (OMe), 66.6 (C-2), 67.3 (C-5), 71.0 (C-4), 99.8 (C-1), 175.2 (CO). ESIMS: $[M + Na]^+$ m/z calcd for $C_9H_{17}NO_5Na$ 242.0999, found 242.0989.

Methyl 3-(3-(*R*)-*t*-butyldimethylsilyloxybutyramido)-2,4-di-*O*-benzyl-3,6-dideoxy-α-D-galactopyranoside (17). 3-(*R*)-*t*-Butyldimethylsilyloxybutanoic acid **16** (66 mg, 0.30 mmol) prepared according to Toriizuka *et al.*,[31] compound **13** (45 mg, 0.125 mmol), DCC (29 mg, 0.134 mmol) and a catalytic amount of DMAP were dissolved in DCM, whereafter the mixture was stirred at r.t. for 3 h. The reaction mixture was filtered, concentrated and recrystallized from ethanol–water to obtain the product as colorless needles (63 mg, 0.11 mmol, 90%). ^{1}H NMR ($CDCl_3$): δ 0.04 (s, 3H, Me–Si), 0.05 (s, 3H, Me–Si), 0.86 (s, 9H, *t*-Bu), 1.13 (d, $J_{H5,H6}$ 6.73 Hz, 3H, Me-6), 1.18 (d, $J_{H3',H4'}$ 6.13 Hz, 3H, Me-4′), 2.17 (m, 2H, CH_2-2′), 3.34 (s, 3H, OMe), 3.75 (dd, $J_{H2,H3}$ 11.30 Hz, $J_{H1,H2}$ 3.42 Hz, 1H, H-2), 3.80 (dd, $J_{H3,H4}$ 3.24 Hz, $J_{H4,H5}$ 1.45 Hz, 1H, H-4), 3.98 (m, 1H, H-3′), 4.43 (ddd, $J_{H2,H3}$ 11.30 Hz, $J_{H3,NH}$ 7.32 Hz, $J_{H3,H4}$ 3.24 Hz, 1H, H-3), 4.56 (d, J_{gem} 11.73 Hz, 1H, $PhCH_2$), 4.58 (n.r., 2H, $PhCH_2$), 4.63 (d, J_{gem} 11.73 Hz, 1H, $PhCH_2$), 4.70 (d, $J_{H1,H2}$ 3.42 Hz, 1H, H-1), 6.15 (d, $J_{H3,NH}$ 7.32 Hz, 1H, NH), 7.28–7.33 (m, 10H, H–Ar). ^{13}C NMR ($CDCl_3$): δ −4.6, −4.5 (2 × Me–Si), 16.7 (C-6), 18.2 (*t*-C), 22.7 (C-4′). 26.0 (Me_3C), 46.1 (CH_2-2′), 50.1 (C-3), 55.3 (OMe), 65.9 (C-5), 66.1 (C-3′), 72.2 ($PhCH_2$), 74.5 (C-2), 76.2 ($PhCH_2$), 79.4 (C-4), 97.7 (C-1), 128.0–128.6 (10 C–Ar), 138.3 (2 × C-*ipso*), 171.0 (CO). ESIMS: $[M + Na]^+$ m/z calcd for $C_{31}H_{47}NSiO_6Na$ 580.3065, found 580.3087.

Methyl 3-(3-(*R*)-hydroxybutyramido)-2,4-di-*O*-benzyl-3,6-dideoxy-α-D-galactopyranoside (18). Compound **17** (31 mg, 0.055 mmol) was dissolved in THF (3 mL), TBAF (35 mg, 0.11 mmol) was added and the mixture stirred for 30 min. The solvent was evaporated under reduced pressure and the crude material was purified by column chromatography (pentane–EtOAc 1 : 1) to obtain the product as a white solid (24 mg, 0.054 mmol, 97%). ^{1}H NMR ($CDCl_3$): δ 1.11, 1.22 (2 × d, J 6.31 Hz, J 6.31 Hz, 2 × 3H, Me-6, Me-4′), 1.82 (m, 2H, CH_2-2′), 3.40 (s, 3H, OMe), 3.59 (d, $J_{H3',OH}$ 2.73 Hz, 1H, OH), 3.71 (dd, $J_{H2,H3}$ 11.32 Hz, $J_{H1,H2}$ 3.36 Hz, 1H, H-2), 3.72 (m, 1H, H-4), 3.99 (m, 2H, H-5, H-3′), 4.38 (d, J_{gem} 11.80 Hz, 1H, $PhCH_2$), 4.39 (m, 1H, H-3), 4.44 (d, J_{gem} 12.30 Hz, 1H, $PhCH_2$), 4.67 (d, J_{gem} 12.30 Hz, 1H, $PhCH_2$), 4.74 (d, J_{gem} 11.80 Hz, 1H, $PhCH_2$), 4.79 (d, $J_{H1,H2}$ 3.36 Hz, 1H, H-1), 5.24 (d, $J_{H3,NH}$ 7.40 Hz, 1H, NH), 7.23–7.35 (m, 10H, H–Ar). ^{13}C NMR ($CDCl_3$): δ 16.7, 22.8 (C-6, C-4′), 43.6 (C-2′), 49.6 (C-3), 55.4 (OMe), 64.8, 66.1 (C-5, C-3′), 72.3 ($PhCH_2$), 74.1 (C-2), 76.4 ($PhCH_2$), 80.2 (C-4), 97.6 (C-1), 128.1–128.8 (10 C–Ar), 138.3, 138.5 (2 × C-*ipso*), 172.5 (CO). ESIMS: $[M + Na]^+$ m/z calcd for $C_{25}H_{33}NO_6Na$ 466.2200, found 466.2207.

Methyl 3-(3-(*R*)-hydroxybutyramido)-3,6-dideoxy-α-D-galactopyranoside (3). Compound **17** (24 mg, 0.054 mmol) was dissolved in 4 mL EtOAc–EtOH 1 : 1, and deprotected as for compound **14** to obtain the product as a white solid (8.6 mg, 0.033 mmol, 60%). ^{1}H NMR (D_2O): δ 1.22 (d, $J_{H5,H6}$ 6.56 Hz, 3H, Me-6), 1.24 (d, $J_{H3',H4'}$ 6.30 Hz, 3H, Me-4′), 2.47 (dd, $J_{H2'a,H2'b}$ −14.11 Hz, $J_{H2'a,H3'}$ 5.02 Hz, 1H, H-2′a), 2.49 (dd, $J_{H2'a,H2'b}$ −14.11 Hz, $J_{H2'b,H3'}$ 8.28 Hz, 1H, H-2′b), 3.44 (s, 3H, OMe), 3.74 (dd, $J_{H3,H4}$ 3.07 Hz, $J_{H4,H5}$ 1.13 Hz, 1H, H-4), 3.85 (dd, $J_{H2,H3}$ 11.14 Hz, $J_{H1,H2}$ 3.84 Hz, 1H, H-2), 4.13 (dd, $J_{H4,H5}$ 1.13 Hz, $J_{H5,H6}$ 6.56 Hz, 1H, H-5), 4.19 (dd, $J_{H2,H3}$ 11.14 Hz, $J_{H3,H4}$ 3.07 Hz, 1H, H-3), 4.23 (ddd, $J_{H2'b,H3'}$ 8.28 Hz, $J_{H2'a,H3'}$ 5.02 Hz, $J_{H3',H4'}$ 6.30 Hz, 1H, H-3′), 4.80 (d, $J_{H1,H2}$ 3.84 Hz, 1H, H-1). ^{13}C NMR (D_2O): δ 16.0 (C-6), 22.7 (C-4′), 45.5 (C-2′), 52.0 (C-3), 55.9 (OMe), 65.9 (C-3′), 66.6 (C-2), 67.3 (C-5), 71.1 (C-4), 99.9 (C-1), 175.0 (CO). ESIMS: $[M + Na]^+$ m/z calcd for $C_{11}H_{21}NO_6Na$ 286.1261, found 286.1248.

Methyl 3-(4-*t*-butyldimethylsilyloxybutyramido)-2,4-di-*O*-benzyl-3,6-dideoxy-α-D-galactopyranoside (20). 4-*t*-Butyldimethylsilyloxybutanoic acid **19** (33 mg, 0.15 mmol) prepared according to Brewer *et al.*,[31,32] compound **13** (45 mg, 0.125 mmol), DCC (29 mg, 0.134 mmol) and a catalytic amount of DMAP were dissolved in DCM and stirred at r.t. for 3 h. The reaction mixture was filtered, concentrated and recrystallized from ethanol–water to obtain the product as a white solid (62 mg, 0.11 mmol, 89%). ^{1}H NMR ($CDCl_3$): δ 0.03 (s, 6H, Me_2Si), 0.89 (s, 9H, *t*-Bu), 1.19 (d, $J_{H5,H6}$ 6.63 Hz, 3H, Me-6), 1.66 (m, 2H,

CH_2-3′), 1.89 (m, 2H, CH_2-2′), 3.38 (s, 3H, OMe), 3.56 (ddd, *J* 1.40 Hz, 6.29 Hz, 7.52 Hz, 2H, CH_2-4′), 3.72 (dd, $J_{H2,H3}$ 10.90 Hz, $J_{H1,H2}$ 3.30 Hz, 1H, H-2), 3.80 (dd, $J_{H3,H4}$ 3.15 Hz, $J_{H4,H5}$ 1.12 Hz, 1H, H-4), 3.99 (m, 1H, H-5), 4.35 (ddd, $J_{H2,H3}$ 10.90 Hz, $J_{H3,NH}$ 7.15 Hz, $J_{H3,H4}$ 3.15 Hz, 1H, H-3), 4.40 (d, J_{gem} 11.90 Hz, 1H, $PhCH_2$), 4.46 (d, J_{gem} 12.30 Hz, 1H, $PhCH_2$), 4.66 (d, J_{gem} 12.30 Hz, 1H, $PhCH_2$), 4.67 (d, J_{gem} 11.90 Hz, 1H, $PhCH_2$), 4.78 (d, $J_{H1,H2}$ 3.30 Hz, 1H, H-1), 5.11 (d, $J_{H3,NH}$ 7.15 Hz, 1H, NH), 7.21–7.35 (m, 10H, H–Ar). ^{13}C NMR ($CDCl_3$): δ −5.2 (2 × Me–Si), 16.7 (C-6), 18.4 (*t*-C), 26.1 (*t*-Bu), 28.7 (C-3′), 33.0 (C-2′), 49.9 (C-3), 55.3 (OMe), 62.4 (C-4′), 66.0 (C-5), 72.0 ($PhCH_2$), 73.7 (C-2), 76.2 ($PhCH_2$), 79.8 (C-4), 97.6 (C-1), 128.0–128.7 (10 C–Ar), 138.2, 138.4 (2 × C-*ipso*), 172.9 (CO). ESIMS: $[M + Na]^+$ *m*/*z* calcd for $C_{31}H_{47}NSiO_6Na$ 580.3065, found 580.3052.

Methyl 3-(4-hydroxybutyramido)-2,4-di-*O*-benzyl-3,6-dideoxy-α-D-galactopyranoside (21). Compound **20** (45 mg, 0.081 mmol) was dissolved in THF (5 mL), TBAF (51 mg, 0.16 mmol) was added and the mixture was stirred for 1 h. The solvent was evaporated under reduced pressure and the crude material was purified by column chromatography (pentane–EtOAc 1 : 4) to obtain the product as a white solid (25 mg, 0.056 mmol, 70%). ^{1}H NMR ($CDCl_3$): δ 1.22 (d, $J_{H5,H6}$ 6.63 Hz, 3H, Me-6), 1.67 (m, 2H, CH_2-3′), 1.83 (m, 1H, H-2′a), 1.95 (m, 1H, H-2′b), 2.75 (n.r., 1H, OH), 3.40 (s, 3H, OMe), 3.56 (m, 2H, CH_2-4′), 3.71 (dd, $J_{H2,H3}$ 11.18 Hz, $J_{H1,H2}$ 3.40 Hz, 1H, H-2), 3.75 (dd, $J_{H3,H4}$ 3.18 Hz, $J_{H4,H5}$ 1.18 Hz, 1H, H-4), 3.99 (m, 1H, H-5), 4.35 (ddd, $J_{H2,H3}$ 11.18 Hz, $J_{H3,NH}$ 7.37 Hz, $J_{H3,H4}$ 3.18 Hz, 1H, H-3), 4.37 (d, J_{gem} 11.90 Hz, 1H, $PhCH_2$), 4.44 (d, J_{gem} 12.24 Hz, 1H, $PhCH_2$), 4.67 (d, J_{gem} 12.24 Hz, 1H, $PhCH_2$), 4.74 (d, J_{gem} 11.90 Hz, 1H, $PhCH_2$), 4.80 (d, $J_{H1,H2}$ 3.40 Hz, 1H, H-1), 5.19 (d, $J_{H3,NH}$ 7.37 Hz, 1H, NH), 7.22–7.36 (m, 10H, H–Ar). ^{13}C NMR ($CDCl_3$): δ 16.7 (C-6), 27.9 (C-3′), 34.0 (C-2′), 49.9 (C-3), 55.4 (OMe), 62.5 (C-4′), 66.1 (C-5), 72.1 ($PhCH_2$), 73.9 (C-2), 76.3 ($PhCH_2$), 80.1 (C-4), 97.6 (C-1), 128.0–128.8 (10 C–Ar), 138.2, 138.5 (2 × C-*ipso*), 173.5 (CO). ESIMS: $[M + Na]^+$ *m*/*z* calcd for $C_{25}H_{33}NO_6Na$ 466.2200, found 466.2201.

Methyl 3-(4-hydroxybutyramido)-3,6-dideoxy-α-D-galactopyranoside (4). Compound **21** (25 mg, 0.056 mmol) was dissolved in EtOH (4 mL) and deprotected as for compound **14** to obtain the product as a white solid (11 mg, 0.042 mmol, 74%).^{1}H NMR (D_2O): δ 1.21 (d, $J_{H5,H6}$ 6.56 Hz, 3H, Me-6), 1.85 (ddddd, $J_{H2'b,H3'a}$ 7.78 Hz, $J_{H2'a,H3'a}$ 8.53 Hz, $J_{H3'a,H3'b}$ −11.29 Hz, $J_{H3'a,H4'a}$ 6.57 Hz, $J_{H3'a,H4'b}$ 5.68 Hz, 1H, H-3′a), 1.85 (ddddd, $J_{H2'b,H3'b}$ 6.61 Hz, $J_{H2'a,H3'b}$ 7.37 Hz, $J_{H3'a,H3'b}$ −11.29 Hz, $J_{H3'b,H4'a}$ 7.91 Hz, $J_{H3'b,H4'b}$ 5.88 Hz, 1H, H-3′b), 2.38 (ddd, $J_{H2'a,H2'b}$ −12.00 Hz, $J_{H2'a,H3'a}$ 8.53 Hz, $J_{H2'a,H3'b}$ 7.37 Hz, 1H, H-2′a), 2.38 (ddd, $J_{H2'a,H2'b}$ −12.00 Hz, $J_{H2'b,H3'a}$ 7.78 Hz, $J_{H2'b,H3'b}$ 6.61 Hz, 1H, H-2′b), 3.44 (s, 3H, OMe), 3.62 (ddd, $J_{H3'a,H4'a}$ 6.57 Hz, $J_{H3'b,H4'a}$ 7.91 Hz, $J_{H4'a,H4'b}$ −9.48 Hz, 1H, H-4′a), 3.62 (ddd, $J_{H3'a,H4'b}$ 5.68 Hz, $J_{H3'b,H4'b}$ 5.88 Hz, $J_{H4'a,H4'b}$ −9.48 Hz, 1H, H-4′b), 3.73 (dd, $J_{H3,H4}$ 3.11 Hz, $J_{H4,H5}$ 1.24 Hz, 1H, H-4), 3.85 (dd, $J_{H2,H3}$ 11.18 Hz, $J_{H1,H2}$ 3.85 Hz, 1H, H-2), 4.11 (dd, $J_{H4,H5}$ 1.24 Hz, $J_{H5,H6}$ 6.56 Hz, 1H, H-5), 4.17 (dd, $J_{H2,H3}$ 11.18 Hz, $J_{H3,H4}$ 3.11 Hz, 1H, H-3), 4.80 (d, $J_{H1,H2}$ 3.85 Hz, 1H, H-1). ^{13}C NMR (D_2O): δ 16.0 (C-6), 28.6 (C-3′), 33.1 (C-2′), 52.0 (C-3), 55.9 (OMe), 61.6 (C-4′), 66.5 (C-2), 67.3 (C-5), 71.1 (C-4), 99.8 (C-1), 177.4 (CO). ESIMS: $[M + Na]^+$ *m*/*z* calcd for $C_{11}H_{21}NO_6Na$ 286.1261, found 286.1247.

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