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Note

Synthesis of 2,6-dideoxy-2-(*N*-methylacetamido)-D-galactose (*N*-acetyl-*N*-methyl-D-fucosamine) and of derivatives suitable for 3-*O*- or 4-*O*-glycosylation †

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2,6-Dideoxy-2-(*N*-methylacetamido)galactose (*N*-acetyl-*N*-methylfucosamine) has been identified [2] in certain type-specific polysaccharides of some *Bordetella pertussis* endotoxin preparations where it is substituted on O-3 by 2,3-diacetamido-2,3-dideoxy-β-D-mannuronic acid and substitutes O-4 of a D-glucosamine residue [3]. 2-Amino-2,6-dideoxy-D- and -L-galactose (D- and L-fucosamine) have been identified as components of many bacterial polysaccharides [4] and have even been found together in the same O-specific polysaccharide of two serogroups of *Pseudomonas aeruginosa* [4]. Syntheses of both enantiomers have been described [5–9]. To our knowledge, the presence of the *N*-methylacetamido sugar in endotoxic lipopolysaccharides had not been previously reported, nor has its synthesis been described.

For comparison and enantiomeric assignment, we required an authentic reference sample of 2,6-dideoxy-2-(*N*-methylacetamido)-D-galactose. Moreover, for projected syntheses of oligosaccharide epitopes containing this sugar, gram-scale quantities of suitable derivatives were needed. *N*-Acetyl-D-glucosamine is the most accessible starting material; it has been used for syntheses of *N*-acetyl-D-fucosamine [7,9] and its derivatives. Two previous syntheses [9,10] of derivatives of *N*-acetyl-D-fucosamine involved etherification of the 3-hydroxyl group of a 4,6-acetal of methyl [10] or benzyl [7,9] glycosides of *N*-acetyl-D-glucosamine, hydrolytic cleavage of the acetal group, methanesulfonylation of the 4 and 6 hydroxyl groups, selective deoxygenation of position 6 [11], and inversion of configuration at C-4 by

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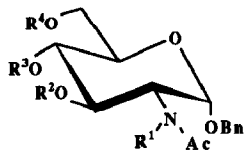
an S_N2 displacement. For the present synthesis, the benzyl glycoside was the obvious choice because of the need to have an aglycon easily removable under mild conditions at the last stage of the synthesis either of the free sugar or of a di- or tri-saccharide in which *N*-acetyl-*N*-methyl-D-fucosamine is the terminal, reducing sugar. It was also necessary that the ether substituent at position 3 be stable under the conditions of *N*-methylation and be susceptible to selective removal leaving the aglycon intact. The latter condition excluded the previously employed [9,12,13] benzyl group since, although selective hydrogenolytic removal of a 3-*O*-benzyl group from some benzyl *N*-acetyl-α-D-fucosamine derivatives has been reported [12,13], a similar selectivity could not be predicted for other derivatives. Instead, we used the 4-methoxybenzyl group, which can be removed selectively under mild conditions in the presence of a benzyl group [14,15] and thus fulfils all of the above requirements. This etherification was performed with 4-methoxybenzyl chloride, under phase transfer conditions, in preference to the less stable and not commercially available bromide, used previously [10] with sodium hydride for a similar synthesis. Inversion of configuration at C-4 by an S_N2 displacement with sodium benzoate [9,16,17] was expected to afford a 4-*O*-benzoyl *galacto* sugar in which the protecting groups at positions 3 and 4 would be independently removable, thus enlarging the synthetic utility of the final, fully protected *N*-methylacetamido-D-fucopyranoside **6**.

Benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside [18] (**1**), obtained uncontaminated by the β anomer (^{1}H NMR) from *N*-acetyl-D-glucosamine by the method of Gross and Wimpler [19], was 3-*O*-methoxybenzylated and the resulting ether **2** (95%) was *N*-methylated by the Hakomori procedure [20]. Removal of the benzylidene group from the *N*-methylacetamido derivative **3** followed by methanesulfonylation of the 4 and 6 hydroxyl groups (cf. ref 10) afforded the 4,6-dimesylate **4** (75%). Attempted deoxygenation of position 6 with sodium borohydride in dimethyl sulfoxide [9,10] failed, but succeeded in hexamethylphosphoric triamide (HMPT) and afforded the 6-deoxy sugar **5** in 85% yield (Weidmann et al. [11] reported a similar result with these two solvents on attempted reductive cleavage of the primary mesyloxy group in benzyl 2-benzamido-2-deoxy-3,4,6-tri-*O*-methanesulfonyl-α-D-glucopyranoside). Treatment of the 4-*O*-mesyl sugar **5** with sodium benzoate in HMPT afforded the 4-*O*-benzoyl *galacto* sugar **6**.

Since compounds **3**–**15** carry a nitrogen group which bears three different substituents, they might be expected to consist of geometrical isomers, provided that pyramidal inversion was restricted. Indeed, a consequence of the restricted or at least slow "umbrella effect" was observed in all of the ^{1}H and ^{13}C NMR spectra, which are each composed of signals corresponding to two compounds. Data obtained by a combination of ^{1}H NMR (COSY) and ^{13}C NMR spectroscopy permitted the assignment of all resonances of both geometrical isomers present in **6**, the only compound analysed in complete detail. (The appearance of two signals for each *N*-acetyl and each *N*-methyl group in the ^{1}H NMR spectra of 2- and 4-(*N*-methylacetamido) deoxy sugars has been reported [21,22], but no indication of the existence of a double set of resonances for other protons was given.)

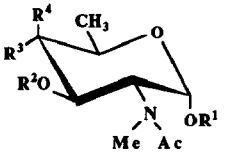


1 $R^1 = R^2 = H$; $R^3, R^4 = CHC_6H_5$

2 $R^1 = H$; $R^2 = MBn$; R^3, R^4 CHC_6H_5

3 $R^1 = Me$; $R^2 = MBn$; $R^3, R^4 = CHC_6H_5$

4 $R^1 = Me$; $R^2 = MBn$; $R^3 = R^4 = Ms$



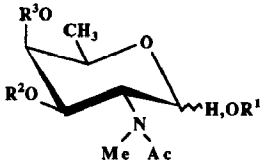
5 $R^1 = Bn$; $R^2 = MBn$; $R^3 = OMs$; $R^4 = H$

6 $R^1 = Bn$; $R^2 = MBn$; $R^3 = H$; $R^4 = OBz$

7 $R^1 = Bn$; $R^2 = R^3 = H$; $R^4 = OBz$

8 $R^1 = Bn$; $R^2 = MBn$; $R^3 = H$; $R^4 = OH$

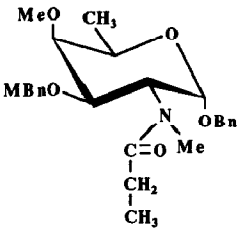
14 $R^1 = Bn$; $R^2 = MBn$; $R^3 = H$; $R^4 = OMe$



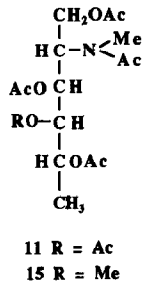
9 $R^1 = R^2 = R^3 = H$

10 $R^1 = Me$; $R^2 = R^3 = H$

12 $R^1 = Me$; $R^2 = R^3 = Ac$



13



11 R = Ac

15 R = Me

MBn = 4-methoxybenzyl

Scheme 1.

Treatment of **6** with ceric ammonium nitrate [14] yielded the 3-hydroxy derivative **7**; de-esterification of **6** with methanolic sodium methoxide gave the 4-hydroxy compound **8**, thus affording acceptors suitable for 3- and 4-glycosylation, respectively. Hydrogenolysis of **8** led to the free sugar **9**, which was very sensitive to acid-catalysed glycosidation as seen by its spontaneous transformation into a mixture of methyl glycosides **10** (characterised by ^1H NMR of their diacetates **12**) during the course of hydrogenation in methanol in the presence of palladium-on-charcoal (Aldrich) despite the fact that the mixture contained no acid other than the traces generated from the catalyst during the hydrogenation. Borohydride reduction of **9** followed by acetylation yielded the *O*-acetylated alditol **11**. The ^1H NMR spectrum of **11** was in conformity with the proposed structure as was the mass spectrum which showed characteristic primary ions [23,24] at, *inter alia*, *m/z* 231 (M − 158, C-3–C-6) and 158 (C-1–C-2, $AcOCH_2CHMeAc^+$)—a diagnostic ion for 2-deoxy-2-(*N*-methylacetamido)alditol acetate derivatives.

In order to obtain a reference compound for methylation analyses of polysaccharides containing 3-*O*-substituted *N*-acetyl-*N*-methylfucosamine, **8** was methylated by the Hakomori procedure [20]. This reaction led not only to the desired 4-methyl ether **14** but also to a substantial amount (~ 50%) of the side product **13**.

Assignment of the *N*-methylpropionamido structure to compound **13** was made on the basis of its spectral data. In the EI mass spectrum of **13**, the molecular ion at *m/z* 457 was 14 mu higher than that of the *N*-methylacetamido compound **14** (443). Moreover, a primary fragment ion at *m/z* 400, present in the spectrum of **14** and attributable to the loss of the *N*-acetyl group (43 amu), is also present (in comparable intensity) in the spectrum of **13** and corresponds to the formal loss of a propionyl group (mu 57). In the IR spectrum, a band at 1634 cm^{-1} confirmed the presence of an amide function. In the ^1H spectrum, in which two geometrical isomers were evident, a multiplet at δ 1.1 and another at δ 2.33 were those expected for a CH_3CH_2 group, and signals at δ 9.23, 9.70, and 26.9, 27.4 in the ^{13}C spectrum confirmed the presence of this group. This spectrum also showed signals for a carbonyl group at δ 175.4 and 178.2. A similar *C*-alkylation of an *N*-methylacetamido group during Hakomori methylation has been observed previously [25] and the possibility of this reaction occurring during methylation analyses of lipopolysaccharides containing *N*-methylacetamido sugars should not be overlooked. Hydrogenation of **14** in ethyl acetate–methanol–water in the presence of palladium-on-charcoal catalyst (in these conditions, the formation of methyl glycosides was not observed although the mixture was slightly acidic at the end of the reaction), followed by reduction and acetylation of the resulting free sugar afforded the pure (TLC and GLC) acetylated 4-*O*-methylalditol **15**, the mass spectrum of which showed, *inter alia*, characteristic primary ions [23,24] at *m/z* 288 (C-2–C-6), 274 (C-1–C-4), 158 (C-1–C-2), and 131 (C-4–C-6), a specific primary fragment of 4-*O*-methylated **15** absent from the spectrum of **11**.

1. Experimental

General methods.—Evaporations were carried out under reduced pressure at 40°C. Mp's were determined on a Kofler hot plate and are uncorrected. Optical rotations were determined with a Perkin–Elmer model 141 polarimeter; values are given for 1% $CHCl_3$ solutions, with the exception of the free sugar, at 23°C. Except where mentioned, all ^1H NMR spectra were recorded on a Bruker AC 200 spectrometer; ^{13}C NMR (50 MHz) and ^1H COSY spectra were recorded on the same instrument, with $CDCl_3$ as solvent (internal Me_4Si) in all cases. EI-mass spectra of glycosides were recorded following direct introduction with a source temperature of 250°C at 70 eV; those of the alditol acetates were obtained by GLC–MS (DB 5 capillary column, 150°C for 2 min then 1°C/min to 260°C). IR spectra were recorded on a Perkin–Elmer 841 spectrometer. TLC was performed on silica gel (60 F_{254} on aluminium foil, Merck); all compounds were located with a UV lamp, where applicable, and by spraying with 10% H_2SO_4 in EtOH and heating on a hot plate. Unless otherwise mentioned, organic solutions were washed with iced water, iced aq 1% H_2SO_4, satd aq $NaHCO_3$, and water, and dried (Na_2SO_4). The solutions were concentrated, the residues, unless crystalline, were subjected to column chromatography on silica gel (Merck 60, 70–230 mesh), and, after removal of the solvents, the eluted products were dried in vacuo (P_2O_5).

Benzyl 2-acetamido-4,6-O-benzylidene-2-deoxy-3-O-(4-methoxybenzyl)-α-D-glucopyranoside (**2**).—A mixture of **1** [10] (6 g, 15mmol), CH_2Cl_2 (300 mL), tetrabutylammonium bromide (2.64 g, 8.2 mmol), 4-methoxybenzyl chloride (8.7 mL, 65.25 mmol), and aq 20% NaOH (15 mL) was stirred vigorously at 40°C until TLC (20:1 $CHCl_3$–EtOH) showed the reaction to be complete (~ 24 h). The cooled mixture was diluted with CH_2Cl_2 (400 mL), and the solution was washed with water and dried (Na_2SO_4). The residue remaining after removal of the solvents was triturated with hexane, and the crystals formed (7.4 g, 95%) were filtered off, washed with hexane, and dried, affording practically pure **2** (TLC) which was used directly for the next step. A sample, recrystallised from $CHCl_3$–hexane, had mp 256–258°C (dec); $[\alpha]_D$ +116°. ^{1}H NMR: δ 1.83 (s, 3 H, NAc), 3.72 (s, 3 H, OMe), 4.85 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 5.05 (s, 1 H, H-acetal), 6.77–7.45 (m, 14 H, aromatic). Anal. Calcd for $C_{30}H_{33}NO_7 \cdot 0.5H_2O$ (528.6): C, 68.17; H, 6.48; N, 2.65. Found: C, 68.15; H, 6.44; N, 2.68.

Benzyl 4,6-O-benzylidene-2-deoxy-3-O-(4-methoxybenzyl)-2-(N-methylacetamido)-α-D-glucopyranoside (**3**).—Sodium methylsulfinylmethanide (dimsyl sodium) [prepared from NaH (2.5 g) and Me_2SO (50 mL)] (33 mL) was added dropwise to a stirred suspension of **2** (7.8 g, 15 mmol) in Me_2SO (40 mL) under Ar. After 24 h, the solution was cooled in an ice bath, CH_3I (34 mL) was added dropwise, and the mixture was allowed to attain room temperature. It was diluted with $CHCl_3$ and worked up in the usual manner. Purification of the residue (column 45 × 4.5 cm) (7:3 EtOAc–cyclohexane) gave **3** (6.1 g, 76%) as a hard oil; $[\alpha]_D$ +95°. ^{1}H NMR: δ 1.96 and 2.08 (2 s, ratio ~ 3.5:1, 3 H, NAc), 2.75 and 2.86 (2 s, ratio ~ 3.5:1, 3 H, NMe), 3.71 (s, 3 H, OMe), 5.54 (s, 1 H, H-acetal), 6.67–7.44 (m, 14 H, aromatic). Anal. Calcd for $C_{31}H_{35}NO_7 \cdot 0.5H_2O$ (542.3): C, 68.60; H, 6.69; N, 2.58. Found: C, 68.70; H, 6.79; N, 2.53.

Benzyl 2-deoxy-4,6-di-O-methanesulfonyl-3-O-(4-methoxybenzyl)-2-(N-methylacetamido)-α-D-glucopyranoside (**4**).—A stirred solution of **3** (5.1 g, 9.5 mmol) in aq 60% AcOH (170 mL) was heated at 80°C for 25 min, cooled, and evaporated to dryness. Toluene was evaporated twice from the residue which was then dissolved in pyridine (35 mL), and methanesulfonyl chloride (10 mL, 125.25 mmol) was added dropwise under Ar to the stirred solution at 0°C. The solution was allowed to attain room temperature and after 2 h was poured into a vigorously stirred mixture of ice–water. After 2–3 h, the mixture was extracted with CH_2Cl_2 and worked up in the usual manner. Purification of the residue (column 46 × 4.5 cm) (7:3 EtOAc–cyclohexane) gave **4** (4.3 g, 75%) as a hard oil; $[\alpha]_D$ +85°. ^{1}H NMR: δ 1.97 and 2.1 (2 s, ratio ~ 7:3, 3 H, NAc), 2.86, 2.89, 2.91, and 2.94 (4 s, 6 H, NMe and 1 $MeSO_2$), 3.01 and 3.02 (2 s, 3 H, 1 $MeSO_2$), 3.7 (s, 3 H, OMe), 3.85 (dd, ~ 0.3 H, $J_{1,2}$ 4, $J_{2,3}$ 12 Hz, H-2), 3.9–4.85 (m, 5 H, H-3,4,5,6,6′), 4.91 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 5.02 (dd, ~ 0.7 H, $J_{1,2}$ 4, $J_{2,3}$ 12 Hz, H-2), 6.72 (d, 2 H, *J* 9 Hz, PMB H-Ar), 7.1 (d, 2 H, *J* 9 Hz, MBn H-Ar), 7.2–7.4 (m, 5 H, Ar). Anal. Calcd for $C_{26}H_{35}NO_{11}S_2$ (601.7): C, 51.90; H, 5.86; N, 2.33. Found: C, 51.95; H, 5.92; N, 2.41.

Benzyl 2,6-dideoxy-4-O-methanesulfonyl-3-O-(4-methoxybenzyl)-2-(N-methylacetamido)-α-D-glucopyranoside (**5**).—A mixture of **4** (4 g, 6.65 mmol), HMPT (23

mL), and $NaBH_4$ (1.04 g) was heated with stirring under Ar at 85°C for 1.5 h; TLC (7:3 EtOAc–cyclohexane) then showed the reaction to be complete. The cooled mixture was poured slowly into aq 1% AcOH (100 mL) with stirring. When **5** had completely solidified, it was filtered off, washed with water, and dissolved in $CHCl_3$, and the solution was dried (Na_2SO_4). The residue (2.98 g, 88%) was sufficiently pure for the next step. A sample, recrystallised from $CHCl_3$–hexane, had mp 163–164°C; $[\alpha]_D$ +101°. ^1H NMR (250 MHz): δ 1.32 (d, 3 H, H-6), 1.97 and 2.1 (2 s, ratio ~7:3, 3 H, NAc), 2.82 and 2.85 (2 s, ratio ~3:7, 3 H, NMe), 2.91 and 2.94 (2 s, ratio ~7:3, 3 H, $MeSO_2$), 3.71 (s, 3 H, OMe), 3.8–4.62 (3 m, ~6.3 H, H-2,3,4, and 2 CH_2Ar), 4.83 (2 d, 1 H, $J_{1,2}$ 4 Hz, H-1), 5.0 (dd, ~0.7 H, $J_{2,3}$ 12 Hz, H-2), 6.77 (d, 2 H, MBn H-Ar), 7.1 (d, 2 H, MBn H-Ar), 7.2–7.3 (m, 5 H, Ar). Anal. Calcd for $C_{25}H_{33}NO_8S \cdot 0.5H_2O$ (516.6): C, 58.12; H, 6.63; N, 2.71. Found: C, 58.21; H, 6.68; N, 2.71.

Benzyl 4-O-benzoyl-2,6-dideoxy-3-O-(4-methoxybenzyl)-2-(N-methylacetamido)-α-D-galactopyranoside (**6**).—A stirred mixture of **5** (5.98 g, 11.8 mmol), HMPT (100 mL), and sodium benzoate (5.87 g, 39.9 mmol) was heated at 140°C under Ar for 24 h. The cooled mixture was poured into ice–water. Solid **6** was filtered off, washed with water, and dissolved in EtOAc, and the solution was dried (Na_2SO_4). The residue was crystallised from EtOAc–hexane to give pure **6** (2.92 g, 47.45%). A further amount of pure **6** (1.83 g) was recovered by column (28 × 3 cm) chromatographic purification of the mother liquors (3:1 $CHCl_3$–Et_2O), bringing the total yield to 76%; **6** had mp 86–87°C; $[\alpha]_D$ +193°. ^1H NMR (400 MHz): δ 1.22 (d, 3 H, H-6), 2.0 and 2.1 (2 s, ratio ~3:1, 3 H, NAc), 2.85 and 2.9 (2 s, ratio ~3:1, 3 H, NMe), 3.75 (s, 3 H, OMe), 4.10 (m, 1 H, $J_{2,3}$ 11, $J_{3,4}$ 2 Hz, H-3), 4.2 (m, 1 H, H-5), 4.26 (d, 1 H, J 11 Hz, CHAr), 4.28 (~0.33 H, H-2), 4.48 and 4.53 (2 d, 2 H, J 11 and 12 Hz, CHAr), 4.98 (d, ~0.33 H, $J_{1,2}$ 3 Hz, H-1), 5.08 (d, ~0.66 H, $J_{1,2}$ 3 Hz, H-1), 5.11 (~0.66 H, $J_{1,2}$ 3, $J_{2,3}$ 11 Hz, H-2), 5.73 (d, ~0.33 H, $J_{3,4}$ 2, $J_{4,5}$ ~0 Hz, H-4), 5.75 (d, ~0.66 H, H-4), 6.8 (d, 2 H, J 9 Hz, MBn H-Ar), 7.1–8.2 (m, 12 H, Ar). Anal. Calcd for $C_{31}H_{35}NO_7$ (533.6): C, 69.78; H, 6.61; N, 2.62. Found: C, 69.65; H, 6.61; N, 2.62.

Benzyl 4-O-benzoyl-2,6-dideoxy-2-(N-methylacetamido)-α-D-galactopyranoside (**7**).—Ceric ammonium nitrate (1.37 g, 2.5 mmol) was added to a solution of **6** (0.67 g, 1.25 mmol) in 9:1 MeCN–H_2O (30 mL), and the mixture was stirred at room temperature until TLC (7:3 EtOAc–cyclohexane) showed the reaction to be complete. CH_2Cl_2 (450 mL) was added and the solution was washed with water, aq 2% $NaHSO_3$, satd aq $NaHCO_3$, and water, and dried. Purification of the residue (column 31 × 2 cm) (7:3 EtOAc–cyclohexane) gave **7** as an oil (0.25 g, 48%); $[\alpha]_D$ +171°. ^1H NMR: δ 1.14 (d, 3 H, H-6), 1.96 (2 s, 3 H, NAc), 2.98 (2 s, 3 H, NMe), 4.15 (m, 1 H, H-5), 4.3 (dd, 1 H, $J_{3,2}$ 12, $J_{3,4}$ 3 Hz, H-3), 4.4 (d, 1 H, J 12 Hz, CHAr), 4.6 (d, 1 H, J 12 Hz, CHAr), 4.9 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 5.0 (dd, 1 H, $J_{1,2}$ 3.5, $J_{2,3}$ 12 Hz, H-2), 5.48 (d, 1 H, $J_{3,4}$ 2 Hz, H-4), 7.23–7.5 (m, 8 H, Ar), 8.15 (d, 2 H, Ar). ^1H NMR after addition in situ of trichloroacetyl isocyanate (esterification of HO-3): δ 1.14 (d, 3 H, H-6), 2.0 (s, 3 H, NAc), 2.9 (s, 3 H, NMe), 4.23 (m, 1 H, H-5), 4.48 (d, 1 H, CHAr), 4.68 (d, 1 H, CHAr), 5.03 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 5.24 (dd, 1 H, $J_{1,2}$ 3.5, $J_{2,3}$ 12 Hz, H-2), 5.57 (m, 2 H, H-3,4), 7.2–7.55 (m, 8

H, Ar), 8.03 (d, 2 H, Ar). Anal. Calcd for $C_{23}H_{27}NO_6 \cdot 0.5H_2O$ (422.5): C, 65.39; H, 6.68; N, 3.31. Found: C, 65.64; H, 6.73; N, 3.28.

Benzyl 2,6-dideoxy-3-O-(4-methoxybenzyl)-2-(N-methylacetamido)-α-D-galactopyranoside (**8**).—A 1 M solution of NaOMe in MeOH (2 mL) was added to **6** (106.8 mg, 0.2 mmol) in MeOH (4 mL); the solution was kept for 24 h at room temperature, neutralised with Amberlite IRN 77 (H^+) resin, filtered, and concentrated to dryness. Purification of the residue (column 12 × 1.2 cm) (8:4:1 EtOAc–hexane–MeOH) gave amorphous **8** (70 mg, 83%); $[\alpha]_D$ +161°. ^{1}H NMR: δ 1.27 (d, 3 H, H-6), 2.02 and 2.06 (2 s, ratio ~0.7:1, 3 H, NAc), 2.78 and 2.85 (2 s, ratio ~1:0.7, 3 H, NMe), 3.75 (s, 3 H, OMe), 3.9 (m, 3 H, H-3,4,5), 4.07 (dd, ~0.3 H, $J_{1,2}$ 3, $J_{2,3}$ 9 Hz, H-2), 4.3–4.65 (m, 4 H, 2 CH_2Ar), 4.9 (m, ~1.7 H, H-1,2), 6.77 (d, 2 H, H-Ar), 7.11–7.27 (m, 7 H, H-Ar). ^{1}H NMR after addition in situ of trichloroacetyl isocyanate: δ 1.2 (d, 3 H, H-6), 1.95 and 2.05 (2 s, ratio ~3:1, 3 H, NAc), 2.75 and 2.8 (2 s, ratio ~3:1, 3 H, NMe), 3.75 (s, 3 H, OMe), 3.95–4.7 (m, ~6.25 H, H-2,3,5, 2 CH_2Ar), 4.85 (m, ~1.75 H, H-1,2), 5.45 (d, 1 H, H-4), 6.75 (d, 2 H, H-Ar), 7.1–7.28 (m, 7 H, H-Ar). Anal. Calcd for $C_{24}H_{31}NO_6$ (429.5): C, 67.11; H, 7.27; N, 3.26. Found: C, 67.02; H, 7.33; N, 3.14.

2,6-Dideoxy-2-(N-methylacetamido)-D-galactose (**9**).—A solution of **8** (83.8 mg) in MeOH containing water (1%) was hydrogenated in the presence of 10% Pd–C. When no more starting material [TLC (8:4:1 EtOAc–hexane–MeOH)] remained and as soon as a secondary product [**10** (double spot), R_f ~0.7 (4:1 $CHCl_3$–MeOH)] started to appear (R_f **9** ~0.5), although a small quantity of UV-absorbing, faster moving material (probably **8** minus the MBn group) remained, the catalyst was filtered off. (In a preliminary experiment, the reaction was left for 48 h, and **9** and **10** were obtained after chromatographic separation in the proportions of 4.7 to 5.2 mg from 25.3 mg of **8**.) Compound **9** (29.4 mg, 68%), purified by column chromatography (4:1 $CHCl_3$–MeOH), had $[\alpha]_D$ +37° (*c* 0.5, H_2O; equilib). Anal. Calcd for $C_9H_{17}NO_5 \cdot 0.5H_2O$ (228.2): C, 47.36; H, 7.95; N, 6.14. Found: C, 47.35; H, 7.94; N, 6.02.

Compound **10** was characterised as its diacetate **12** (see below).

1,3,4,5-Tetra-O-acetyl-2,6-dideoxy-2-(N-methylacetamido)-D-galactitol (**11**) *and methyl di-O-acetyl-2,6-dideoxy-2-(N-methylacetamido)-D-galactosides* (**12**).—Sodium borohydride (9 mg) was added to stirred solutions of **9** (4.7 mg) and **10** (5.2 mg), treated in parallel, in water (1 mL). After 24 h, the solutions were acidified with IRN 77 (H^+) resin, filtered, and evaporated to dryness, and MeOH was evaporated several times from the residues which were then treated for 1 h at 110°C with Ac_2O (0.2 mL)–anhyd NaOAc. Acetic anhydride was removed by successive evaporations with toluene, $CHCl_3$ solutions of the residues were filtered, and solvents were removed. A solution of **11** in EtOAc was filtered through a bed (1.5 × 0.5 cm) of silica gel to remove some UV-absorbing materials, the eluate was concentrated, and the residue was dried. ^{1}H NMR: total 27 H (theoretical 27 H), δ 1.05 (d, H-6), 2.04-2.08 (5 s, 15 H, NAc, 4 OAc), 2.94 (s, 3 H, NMe), 4.05 (m, 2 H, CH_2OAc), 4.93 (m, 2 H, H-4,5), 5.27 (m, 1 H, H-2), 5.43 (dd, 1 H, H-3). GLC (single peak t_R 35.4 min)-MS: *m/z* 330 (1.1% of base peak 116, M − 59), 329 (1.5%, M − 60), 316 [6%, M − 73 (M − C-1)], 302 [3%, M − 87

(M – C-5–C-6), 231 [0.4%, M – 158 (C-3–C-4–C-5–C-6)], 230 (0.4%, M – 159), 159 (7.4%, C-4–C-5–C-6), 158 (86%, C-1–C-2), 116 (100%, 158 – 42), 98 (9%, CH_2=CNMeAc), 87 (3%, C-5–C-6). ^{1}H NMR of **12**: total 23 H (theoretical 23 H), δ 1.2 (m, 3 H, H-6), 2.05 (m, 9 H, NAc, 2 OAc), 2.74, 2.87, and 2.98 (3 s, 3 H, NMe), 3.32 and 3.46 (4 s, 3 H, OMe), 3.7–5.2 (5 H, H-1,2,3,4,5). GLC (BP 10 capillary column, isothermal at 180°C): two incompletely resolved peaks at t_R 23.85 and 24.2 min. MS: *m/z* 286 (1% of base peak 43, M – 31), 244 (18% M – NHMeAc).

*Benzyl 2,6-dideoxy-3-*O*-(4-methoxybenzyl)-4-*O*-methyl-2-(*N*-methylpropionamido)-α-*D*-galactopyranoside* (**13**) *and benzyl 2,6-dideoxy-3-*O*-(4-methoxybenzyl)-4-*O*-methyl-2-(*N*-methylacetamido)-α-*D*-galactopyranoside* (**14**).—Dimsyl sodium (see **3**) (0.5 mL) was added dropwise to a stirred solution of **8** (15.3 mg, 0.0357 mmol) in Me_2SO (1 mL) under Ar. Stirring was continued for 1.5 h, the solution was cooled in an ice bath, CH_3I (0.5 mL) was added dropwise, and the mixture was allowed to attain room temperature. It was poured into cold water which was then extracted with CH_2Cl_2 (4 × 3 mL), and the combined extracts were washed with water and dried. Elution of the residue from a column (45 × 4.5 cm) (7:3 EtOAc–cyclohexane) gave firstly **13** (5.2 mg), $R_f \sim 0.57$. ^{1}H NMR: δ 1.1 (m, 3H, CH_2CH_3), 1.21 (d, 3 H, H-6), 2.33 (m, 2 H, CH_2CH_3), 2.77 and 2.83 (2 s, 3 H, NMe), 3.52 (m and 2 s, 4 H, H-4 and 4-OMe), 3.73 (2 s, 3 H, *Me*OAr), 3.9 (m, 2 H, H-3 and H-5), 4.33 (m, ~2.6 H, H-2, CH_2Ar), 4.58 (m, 2 H, CH_2Ar), 4.82 and 4.9 (2 d, 1 H, $J_{1,2} \sim 3$ Hz, H-1), 5.02 (dd, ~0.4 H, $J_{1,2} \sim 3$, $J_{2,3} \sim 12$ Hz, H-2), 6.8 (d, 2 H, H-Ar), 7.2 (m, 7 H, H-Ar). ^{13}C NMR (Bruker programme "J MODXH.AU"): δ 9.23 and 9.70 (CH_3CH_2), 16.59 and 16.79 (CH_3-6), 26.90 and 27.37 (CH_3CH_2), 29.92 and 31.61 (NCH_3), 52.10 (CH_3OAr), 55.26 and 55.43 (C-2), 61.37 and 61.71 (4-OCH_3), 66.51 (C-5), 74.47 and 74.77 (C-3), 69.55, 69.76, and 70.75 (2 CH_2 of MBn and Bn), 78.16 and 78.43 (C-4), 98.57 and 99.21 (C-1), 113.77 and 113.85 (*o*-CH of MBn), 127.58, 127.86, 128.36, 128.47, 129.11, and 129.20 (CH-Ar), 129.57 and 129.91 (quaternary C attached to CH_2 of MBn), 137.12 and 137.99 (quaternary C of Bn), 157.63 and 159.31 (quaternary C attached to CH_3O of MBn), 175.43 and 178.18 (CO). IR: ν_{max} 1634 cm^{-1} (amide). MS: *m/z* 457 (0.41%, M^+), 400 (0.58%, M – $COCH_2CH_3$), 349 (1.28%, M – $C_6H_5CH_2OH$), 121 (100%, $CH_3OC_6H_4CH_2$).

Compound **14** (4.7 mg), $R_f \sim 0.28$, was the second product to be eluted. ^{1}H NMR: δ 1.24 (d, 3 H, H-6), 2.0 and 2.07 (d, ratio ~0.4:0.6, 3 H, NAc), 2.79 and 2.85 (d, ratio ~0.4:0.6, 3 H, NMe), 3.53 (m and 2 s, 4 H, H-4 and 4-OMe), 3.72 (2 s, 3 H, *Me*OAr), 3.9 (m, 2 H, H-3 and H-5), 4.2 (dd, ~0.6 H, $J_{1,2}$ 3, $J_{2,3}$ 12 Hz, H-2), 4.3–4.7 (m, 4 H, 2 CH_2Ar), 4.84 and 4.92 (2 d, 1 H, $J_{1,2}$ 3 Hz, H-1), 5.05 (dd, ~0.4 H, $J_{1,2}$ 3, $J_{2,3}$ 12 Hz, H-2), 6.8 (d, 2 H, H-Ar), 7.2 (m, 7 H, H-Ar). MS: *m/z* 443 (0.25%, M^+), 400 (0.25%, M – $COCH_3$), 335 (1.28%, M – $C_6H_5CH_2OH$), 121 (100%, $CH_3OC_6H_4CH_2^+$).

*1,3,5-Tri-*O*-acetyl-2,6-dideoxy-4-*O*-methyl-2-(*N*-methylacetamido)-*D*-galactitol* (**15**).—A solution of **14** (4.5 mg) in 8:4:1 EtOAc–MeOH–water was hydrogenated in the presence of Pd–C. When TLC (4:1 $CHCl_3$–MeOH) showed the hydrogenation to be complete, the catalyst was filtered off, the solvents were removed, and $NaBH_4$ (4 mg) was added to a stirred solution of the residue in water (0.5 mL).

After 24 h, the solution was acidified with IRN 77 (H^+) resin, filtered, and evaporated to dryness, and MeOH was evaporated several times from the residue which was then treated for 1 h at 110°C with Ac_2O (0.2 mL)–anhyd NaOAc. Acetic anhydride was removed by successive evaporations with toluene, $CHCl_3$ was added to the residue, solids were filtered off, and the solvent was removed. TLC: single spot R_f 0.5 (8:4:1 EtOAc–hexane–MeOH). GLC (single peak t_R 34 min)–MS: m/z 288 [3.4%, M − 73 (M − C-1)], 274 [6.5%, M − 87 (M − C-5–C-6)], 158 (64%, C-1–C-2), 131 (15%, C-4–C-5–C-6), 116 (100%, 158 − 42), 98 (21%, CH_2=CNMeAc), 87 (4.4%, C-5–C-6).

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