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Synthesis of 3-deoxy-D-*manno*-2-octulosonic acid (Kdo) and D-*glycero*-D-*talo*-2-octulosonic acid (Ko) and their α-glycosides

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Abstract

Reaction of 2,3:5,6-di-*O*-isopropylidene-D-mannofuranose **1** with C-2 lithio derivatives of glyoxylate mercaptal in the presence of $MgBr_2$ afforded D-*glycero*-D-*galacto*-2-octulosonates **2** and **3**, respectively. Their 3-*O*-deoxygenation led to Kdo. *N*-Iodosuccinimide treatment of **3** gave thioglycoside **11** directly**,** which was transformed into Ko derivative **12** via epimerisation of the 3-hydroxy group. 3-*O*-Benzoylation of **12** and then transformation into phosphite furnished **15**, an efficient glycosyl donor. Reaction of **15** with 6-*O*-unprotected glucosamine derivative **22** as acceptor gave α-glycoside **23**, which was successfully transformed either into Kdo-disaccharide **27** or into Ko-disaccharide **29**.

1. Introduction

Kdo is an integral constituent of the lipopolysaccharide (LPS) of Gram-negative bacteria.[1] The difficulty of its isolation out of biological material as well as the desire to study the biological functions of such complex glycoconjugates as LPS led to an increasing interest in short and efficient syntheses of Kdo and its glycosides. Quite a few endeavours in this regard have been reported.[2–4] Some years ago another octolusonic acid derivative, namely Ko (abbreviation taken from D-*glycero*-D-*talo*-2-keto-octosonate), was detected as a constituent of the LPS of *Acinetobacter calcoaceticus* NTC 10305,[5] which has, meanwhile, also been found in other species.[6] Also, syntheses of this compound, particularly employing dihydroxylation or epoxidation of 2,3-dehydro-Kdo derivatives, and the transformation into glycosides has been investigated.[7] We report here on a novel approach to the synthesis of the 2-octulosonate skeleton (Kdo, Ko and the 3-epimer), which can be successfully employed for efficient syntheses of the desired α-glycosides of Ko and Kdo. It is based on nucleophilic acylation of readily available 2,3:5,6-di-*O*-isopropylidene-D-mannose[8] (Scheme 1, **1**) as a C_6-building block with a glyoxylate C-2 carbanion equivalent as a C_2-building block; the C_2-building block is generated through deprotonation

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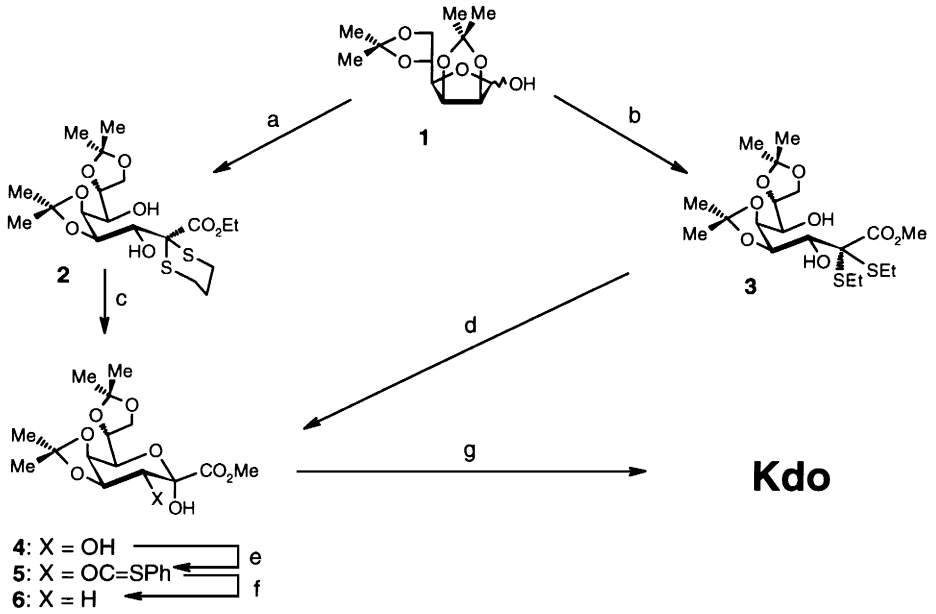
of a mercaptal of glyoxylate[9] (Scheme 1). This approach readily provides an acyloxy function at C-3 of 2-octulosonate which can be used: (i) to generate the 3-hydroxy group of the Ko series; (ii) to provide anchimeric assistance for Ko- and Kdo-α-glycoside bond formation; and (iii) to perform regioselective 3-deoxygenation to give Kdo and its glycosides. Thus, this approach is more versatile and efficient than, for instance, alkylation of the carbanion of glyoxylate mercaptals with mannitol derivatives, which provides Kdo,[10] but does not take into account either the control of α-glycoside bond formation or the need for Ko and its glycosides.



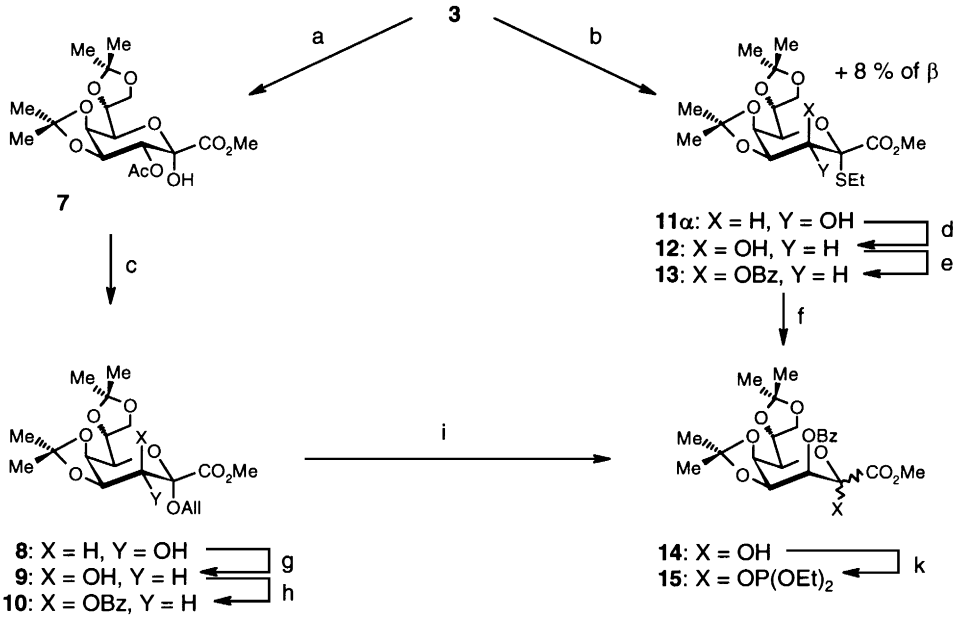
Scheme 1. Reagents and conditions: (a) ethyl 1,3-dithiane-2-carboxylate, LDA, $MgBr_2$, THF; 76%; (b) $(EtS)_2CHCOOMe$, LDA, $MgBr_2$, THF; 76%; (c) NBS, acetone; NaOMe, MeOH; 30%; (d) NIS, acetone; 76%; (e) $PhC(Cl)=NMe_2Cl$, pyridine; CH_2Cl_2; H_2S, AcOH; 80%; (f) Bu_3SnH, AIBN, toluene; 83%; (g) Refs. 2a, 10a

2. Results and discussion

To this end, ethyl 1,3-dithiane-2-carboxylate[11] was treated with lithium diisopropylamide (LDA) in order to generate the 2-lithio derivative. Addition of $MgBr_2$ to this solution[12] and then **1** afforded practically only the D-*glycero*-D-*galacto*-2-octulosonate derivative **2**, the epimer of the corresponding Ko derivative. Variations of the reaction conditions and reagents led to mixtures of the two epimers.[13] A similar result was obtained with methyl glyoxylate diethyl mercaptal,[9] thus providing 2-octulosonate derivative **3** in 76% yield.

Treatment of **3** with *N*-iodosuccinimide (NIS) in acetone led to methyl 2-octulopyranosonate **4**; the same compound was also obtained on reaction of **2** with *N*-bromosuccinimide (NBS) and then transesterification with sodium methanolate in methanol. For Kdo generation, 3-deoxygenation was required, which was performed following Barton's procedure.[14] Therefore, **4** was treated with *N,N*-dimethyl-α-chloro-benzimidium chloride in pyridine and then with hydrogen sulfide in acetic acid to furnish 2-*O*-thiobenzoyl derivative **5**. Treatment of **5** with tributyltin hydride and azoisobutyronitrile (AIBN) afforded known 4,5:7,8-di-*O*-isopropylidene derivative **6** of Kdo;[2a] efficient transformation into Kdo has already been reported.[10a]

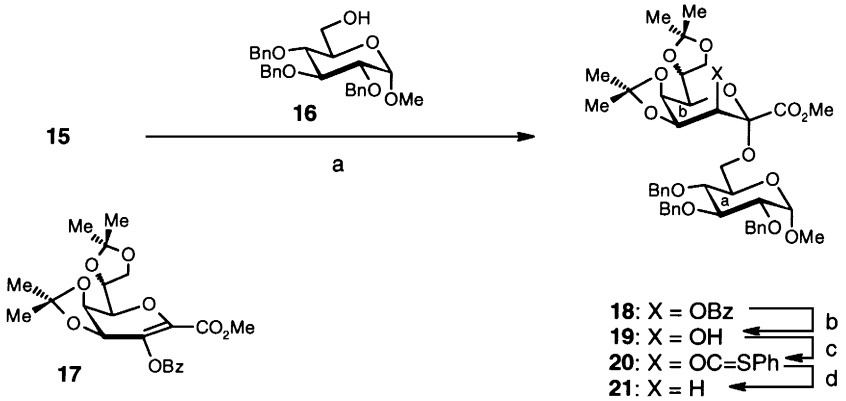
Readily available **3** is also a useful starting material for the generation of glycosyl donors of Ko and Kdo. Treatment of **3** with NIS in acetone and then regioselective 3-*O*-acetylation with acetyl chloride in pyridine gave **7** (Scheme 2). Direct anomeric 2-*O*-allylation with sodium hydride/allyl bromide in DMF[15] and then quenching the reaction mixture with methanol furnished α-anomer **8** exclusively, which could be used for epimerisation at the 3-position. Oxidation with Dess–Martin periodinane[16] and then reduction with the borane–ammonia complex afforded the desired Ko epimer **9**. The configurations of **8** and **9** were confirmed by the NMR data. 3-*O*-Benzoylation of **9** (→**10**) and then removal of the 2-*O*-allyl group was performed as described by Yin et al.,[17] thus affording 2-*O*-unprotected Ko derivative **14**. The same compound was more simply gained from **3** when the NIS reaction was performed in acetonitrile at −30°C, directly furnishing a mixture of the thioglycosides **11** (85%, α:β=10:1), which could be readily separated. Epimerisation of the α-isomer **11** at the 3-position as described above gave Ko epimer **12**. 3-*O*-Benzoylation with benzoyl chloride in the presence of Steglich's base (DMAP) led to thioglycoside **13**, which exhibited only modest glycosyl donor properties.[18] Therefore, **13** was reacted with NIS in acetic acid in the presence of trifluoromethanesulfonic acid (TfOH) to give the known **14** in high overall yield (46% from **3**). Reaction of **14** with diethyl chlorophosphite in the presence of Hünig's base gave phosphite **15** as glycosyl donor in high yield (91%).



Scheme 2. Reagents and conditions: (a) NIS, acetone; AcCl, pyridine, CH_2Cl_2; 70%; (b) NIS, CH_3CN, −30°C; 77%; (c) AllBr, NaH, DMF; MeOH; 72%; (d) Dess–Martin periodinane, CH_2Cl_2; BH_3–NH_3, MeOH; 88%; (e) BzCl, DMAP, CH_2Cl_2; 96%; (f) NIS, TfOH, AcOH, acetone; 70%; (g) Dess–Martin periodinane, CH_2Cl_2; BH_3–NH_3, MeOH; 87%; (h) BzCl, DMAP, CH_2Cl_2; 92%; (i) $Pd(PPh_3)_4$, $ZnCl_2$, Bu_3SnH, THf; $CH_2{=}C(CH_3)OCH_3$, TsOH, acetone; 43%; (k) $(EtO)_2PCl$, Hünig's base, CH_3CN; 91%

The glycosyl donor properties of **15** were investigated with the known 6-*O*-unprotected glucose derivative **16**[19] as acceptor (Scheme 3). Reaction in dichloromethane at −15°C with TMSOTf as catalyst afforded, due to anchimeric assistance of the 3-benzoyloxy group, the desired α-glycoside **18** in good yield; essentially, the only by-product was 2,3-dehydro derivative **17**. Compound **18** can be readily converted into the Ko or into the Kdo disaccharide. Thus, treatment of **18** with sodium methanolate in methanol led to 3b-*O*-debenzoylation (→**19**); transformation into 3-*O*-thiobenzoyl derivative **20** and

then deoxygenation as described above gave known Kdo-disaccharide **21**,[20] thus also confirming the structural assignments.



Scheme 3. Reagents and conditions: (a) TMSOTf, CH_2Cl_2; 62%; (b) NaOMe, MeOH: 90%; (c) $PhC(Cl)=NMe_2Cl$, pyridine, CH_2Cl_2; H_2S, pyridine; 94%; (d) Bu_3SnH, AIBN, toluene; 76%

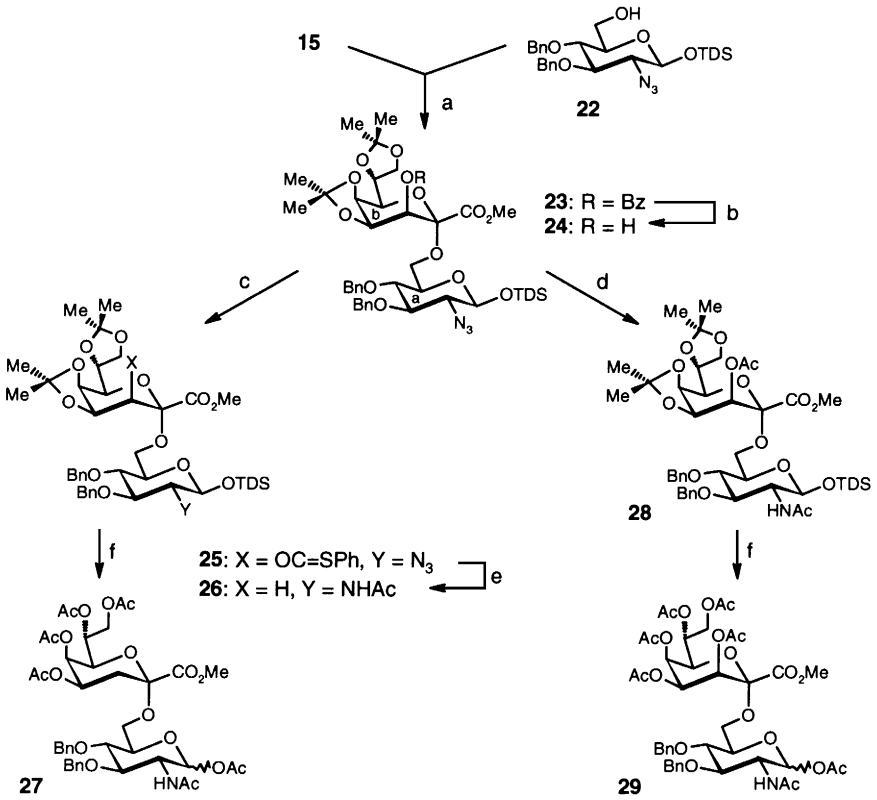
The most important glycosidic linkage of Ko and Kdo is 6-*O*-connection to glucosamine.[1] A versatile acceptor is 2-azido-2-deoxy derivative **22**, which has already been employed with 1-*O*-*tert*-butyldimethylsilyl protection in other approaches to the synthesis of Kdo glycosides[21] (Scheme 4). 1-*O*-Thexyldimethylsilyl (TDS) protected **22** was obtained from the corresponding known 4,6-*O*-benzylidene derivative[22] via reductive ring opening with BH_3/TMSOTf.[23] Glycosidation of **22** with **15** under the above described conditions gave α-linked disaccharide **23**, together with **17**, in good yield. 3b-*O*-Debenzoylation of **23** gave **24**, which served as precursor for the Ko- and the Kdo-disaccharide. 3b-*O*-Thiobenzoylation (→**25**) and deoxygenation was performed as described above, thus leading to concomitant azido group reduction; treatment of the intermediate with acetic anhydride in pyridine gave 2a-acetylamino-2a,3b-dideoxy disaccharide **26**. Acid catalysed de-*O*-isopropylidenation also led to cleavage of the TDS group; subsequent *O*-acetylation gave target molecule **27**, which had NMR data in agreement with those of a structurally closely related Kdo-disaccharide.[22] Azido group reduction of **24** with hydrogen sulfide in pyridine/water and ensuing treatment with acetic anhydride in pyridine gave Ko-disaccharide **28**. De-*O*-isopropylidention and concomitant de-*O*-silylation and then *O*-acetylation under the above described conditions furnished target molecule **29**.

In conclusion, addition of C-2 lithio glyoxylate mercaptals to mannose derivative **1** in the presence of $MgBr_2$ afforded D-*glycero*-D-*talo* compounds **2** and **3**. Compound **3** could be readily transformed into a Ko glycosyl donor, which was successfully employed for the synthesis of Ko- and Kdo-α-disaccharides, respectively.

3. Experimental

3.1. General methods

Solvents were purified and dried in the usual way; boiling range of the petroleum ether: 35–65°C. Thin layer chromatography (TLC): Merck foil plates, silica gel 60 F_{254}. Preparative flash chromatography: J. T. Baker silica gel 60 (30–60 μm) at a pressure of 0.2–0.4 bar. Melting points: Gallenkamp metal block; not corrected. Optical rotation: Perkin–Elmer Polarimeter 241/MS, 1 dm cell. FAB-MS: modified Finnigan MAT 312/AMD-5000 spectrometer; matrix: 3-nitrobenzyl alcohol. MALDI-MS: Kratos Analytic Kom-



Scheme 4. Reagents and conditions: (a) TMSOTf, CH_2Cl_2; 56%; (b) NaOMe, MeOH; 91%; (c) $PhC(Cl)=NMe_2Cl$, pyridine, CH_2Cl_2; H_2S, pyridine; 94%; (d) H_2S, pyridine; H_2O; Ac_2O, DMAP, pyridine; 78%; (e) Bu_3SnH, AIBN, toluene; H_2S, pyridine, H_2O; Ac_2O, pyridine; 70%; (f) CF_3COOH, H_2O, CH_2Cl_2; Ac_2O, pyridine; 55%

pac Maldi 2; matrix: 2,5-dihydroxybenzoic acid. NMR spectra: Bruker AC 250 Cryospek (250 MHz) and Bruker DRX 600 (600 MHz); internal standard: the residual chloroform (δ=7.24 ppm) or DMSO (δ=2.49 ppm).

3.2. *Ethyl 2-deoxy-4,5:7,8-di*-O-*isopropylidene*-D-glycero-D-galacto-*octulosonate 1,3-propylene dithioacetal* ***2***

A solution of diisopropylamine (23.2 mL, 174 mmol) in dry THF (200 mL) was treated with *n*-BuLi (109.0 mL, 1.6 M in hexane, 174 mmol) at −20°C. After stirring for 15 min ethyl 1,3-dithiane-2-carboxylate (25 mL, 159 mmol) was slowly added. The dark red solution was kept for 2 h at −20°C and then added to a cooled suspension of $MgBr_2$ (−20°C) in dry THF (250 mL) made from magnesium (5.8 g, 238 mmol) and 1,2-dibromoethane (18.2 mL, 211 mmol). Then 2,3:5,6-di-*O*-isopropylidene-D-mannose **1** (13.8 g, 53 mmol) was added without any solvent. The reaction mixture was warmed to room temperature over a period of 3 h, stirred for 3 h at 50°C, then poured into ice-cold, satd. aqueous NH_4Cl (500 mL) and extracted with EtOAc (900 mL). The combined extracts were washed with water, dried ($MgSO_4$) and evaporated; the residue was purified by flash chromatography (toluene:EtOAc, 5:1) to afford excess ethyl 1,3-dithiane-2-carboxylate and **2** (18.2 g, 76%) as a light brownish syrup; TLC (toluene:EtOAc, 1:1): R_f 0.54; $[\alpha]_D$ −1.8 (*c* 1, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.32 (t, 3H, *J*=7.4 Hz, $COOCH_2CH_3$), 1.33, 1.35, 1.39, 1.48 [4s, 12H, $C(CH_3)_2$], 1.79–3.27 [m, 6H, $S(CH_2)_3S$], 3.60

(dd, 1H, $J_{4,5}$=1.0 Hz, $J_{5,6}$=6.9 Hz, 5-H), 3.98–4.33 (m, 6H, 6-, 7-, 8-, 8′-H, COOCH_2CH$_3$), 4.40 (dd, 1H, $J_{3,4}$=7.5 Hz, 4-H), 4.54 (d, 1H, 3-H). Anal. calcd for $C_{19}H_{32}O_8S_2$ (452.57): C, 50.42; H, 7.13; found: C, 50.11; H, 7.12.

3.3. *Methyl 2-deoxy-4,5:7,8-di*-O-*isopropylidene*-D-glycero-D-galacto-*octulosonate diethyldithioacetal* ***3***

A solution of diisopropylamine (56.4 mL, 400 mmol) in dry THF (400 mL) was treated with *n*-BuLi (250.0 mL, 1.6 M in hexane, 400 mmol) at −20°C. After stirring for 15 min glyoxylic acid methyl ester diethyl mercaptal (70.5 g, 363 mmol) was slowly added. The dark red solution was kept for 2 h at −20°C and then added to a −20°C cooled suspension of $MgBr_2$ in dry THF (400 mL) made from magnesium (13.3 g, 554 mmol) and 1,2-dibromoethane (41.8 mL, 485 mmol). Then 2,3:5,6-di-*O*-isopropylidene-D-mannose **1** (31.6 g, 121 mmol) was added without any solvent. The reaction mixture was warmed to room temperature over a period of 3 h, stirred for 3 h at 50°C, then poured into ice-cold, satd. aqueous NH_4Cl (1 L) and extracted with EtOAc (2 L). The combined extracts were washed with water, dried ($MgSO_4$) and evaporated; the residue was purified by flash chromatography (toluene:EtOAc, 6:1) to afford **3** (41.8 g, 76%) as a light brownish syrup; TLC (toluene:EtOAc, 1:1): R_f 0.54; $[\alpha]_D$ −59.1 (*c* 1, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.16–1.22 (m, 6H, SCH$_2$CH_3), 1.31, 1.36, 1.45 [3s, 12H, C(CH$_3$)$_2$], 2.50–2.75 (m, 4H, SCH_2CH$_3$), 3.56 (ddd, 1H, $J_{4,5}$=1.0 Hz, $J_{5,6}$=6.7 Hz, $J_{5,6\text{-OH}}$=2.6 Hz, 5-H), 3.74 (s, 3H, COOCH$_3$), 3.82 (d, 1H, 6-OH), 3.93–4.12 (m, 5H, 6-, 7-, 8-, 8′-H, 3-OH), 4.37 (dd, 1H, $J_{3,4}$=7.6 Hz, 4-H), 4.72 (d, 1H, 3-H); MALDI-MS: $[M+Na]^+$=477, $[M+K]^+$=493. Anal. calcd for $C_{19}H_{34}O_8S_2$ (454.59): C, 50.20; H, 7.54; found: C, 50.44; H, 7.56.

3.4. *Methyl 4,5:7,8-di*-O-*isopropylidene*-α-D-glycero-D-galacto-*2-octulopyranosonate* ***4***

I. From **2**: A solution of **2** (150 mg, 330 μmol) in acetone (5 mL) was treated with NBS (210 mg, 1.18 mmol) dissolved in 97% acetone (10 mL), and the reaction mixture was vigorously stirred for 3 min at 0°C. Then satd. aqueous $NaHCO_3$ and satd. aqueous $Na_2S_2O_3$ were added to the reaction mixture and extracted with EtOAc several times. The organic phase was dried ($MgSO_4$) and concentrated to dryness. The residue was dissolved in dry MeOH (5 mL) and treated with 1 M MeONa in MeOH (0.1 mL). The solution was stirred overnight at room temperature, neutralised with Amberlite IR-120 (H^+) resin and filtered. The resin was washed, and the combined filtrate and washings were concentrated. Flash chromatography (toluene:acetone, 5:1) gave **4** as a white solid (35 mg, 30%).

II. From **3**: To a solution of **3** (2.30 g, 4.91 mmol) in 98% acetone (100 mL) was added NIS (2.76 g, 12.28 mmol) at 0°C. After 30 min (monitored by TLC), NEt_3 (5 mL), satd. aqueous $NaHCO_3$ and satd. aqueous $Na_2S_2O_3$ were added to the reaction mixture and extracted with EtOAc three times. The organic phase was dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography of the residue (toluene:acetone, 5:1) afforded **4** as a white solid (1.30 g, 76%); TLC (toluene:EtOAc, 1:1): R_f 0.21; m.p. 128°C; $[\alpha]_D$ +30.2 (*c* 1, $CHCl_3$); ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.25, 1.13, 1.39 [3s, 12H, C(CH$_3$)$_2$], 3.66 (s, 3H, COOCH$_3$), 3.73 (ddd, 1H, $J_{3,3\text{-OH}=}$7.6 Hz, $J_{3,2\text{-OH}=}$1.7 Hz, $J_{3,4=}$7.7 Hz, 3-H), 3.81 (dd, 1H, $J_{8,8'=}$8.4 Hz, $J_{7,8=}$4.7 Hz, 8-H), 3.91 (dd, 1H, $J_{5,6=}$2.4 Hz, $J_{6,7=}$8.6 Hz, 6-H), 3.95 (dd, 1H, $J_{7,8'=}$6.5 Hz, 8′-H), 4.04 (dd, 1H, $J_{4,5=}$5.7 Hz, 4-H), 4.16 (ddd, 1H, 7-H), 4.18 (dd, 1H, 5-H), 5.23 (d, 1H, 3-OH), 6.94 (d, 1H, 2-OH); ^{13}C NMR (150.9 MHz, DMSO-d_6) δ: 25.2, 26.4, 26.6, 28.0 [4C, C(*C*H$_3$)$_2$], 52.2 (1C, COO*C*H$_3$), 66.3 (1C, 8-C), 69.3 (1C, 6-C), 70.1 (1C, 3-C), 72.5 (1C, 5-C), 73.2 (1C, 7-C), 76.4 (1C, 4-C), 95.9 (1C, 2-C), 108.1, 108.5 [2C, *C*(CH$_3$)$_2$], 169.5 (1C, 1-C). Anal. calcd for $C_{15}H_{24}O_9$ (348.35): C, 51.72; H, 6.94; found: C, 51.65: H, 6.83.

3.5. *Methyl 4,5:7,8-di*-O-*isopropylidene-3*-O-*thiobenzoyl*-α-D-glycero-D-galacto-*2-octulopyranosonate* **5**

N,N-Dimethyl-α-chlorobenzimidium chloride (370 mg, 1.81 mmol) was added to a solution of **4** (250 mg, 0.72 mmol) in dry CH_2Cl_2:pyridine (20:1, 10 mL). The mixture was stirred at room temperature overnight, then treated with H_2S, AcOH (10 mL), and again with H_2S. After 3 h, satd. aqueous $NaHCO_3$ was added, and the mixture was extracted with EtOAc. The organic layer was dried ($MgSO_4$), concentrated in vacuo, and the residue was purified by flash chromatography (toluene:EtOAc, 8:1) to give **5** (270 mg, 80%) as a yellow syrup; TLC (toluene:EtOAc, 1:1): R_f 0.66; $[\alpha]_D$ +81.2 (*c* 0.5, $CHCl_3$); ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.27, 1.29, 1.36, 1.48 [4s, 12H, C(CH_3)$_2$], 3.52 (s, 3H, $COOCH_3$), 3.91 (dd, 1H, $J_{7,8}$=4.6 Hz, $J_{8,8'}$=8.5 Hz, 8-H), 4.03 (dd, 1H, $J_{7,8'}$=6.4 Hz, 8′-H), 4.09 (dd, 1H, $J_{5,6}$=2.4 Hz, $J_{6,7}$=8.5 Hz, 6-H), 4.31 (ddd, 1H, 7-H), 4.41 (dd, 1H, $J_{4,5}$=5.3 Hz, 5-H), 4.56 (dd, 1H, $J_{3,4}$=7.5 Hz, 4-H), 6.15 (dd, 1H, $J_{3,OH}$=1.1 Hz, 3-H), 7.74 (d, 1H, OH), 7.48–8.06 (m, 5H, Ph); ^{13}C NMR (150.9 MHz, DMSO-d_6) δ: 25.2, 26.4, 26.7, 27.4 [4C, C(*C*H_3)$_2$], 52.7 (1C, COO*C*H_3), 66.3 (1C, 8-C), 69.1 (1C, 6-C), 72.7 (1C, 5-C), 73.2 (1C, 7-C), 74.0 (1C, 4-C), 78.5 (1C, 3-C), 94.0 (1C, 2-C), 108.7, 109.2 [2C, *C*(CH_3)$_2$], 128.5–137.9 (6C, Ph), 168.0 (1C, 1-C), 211.1 (1C, *C*SPh). Anal. calcd for $C_{22}H_{28}O_9S$ (468.52): C, 56.40; H, 6.02; found: C, 56.41; H, 5.98.

3.6. *Methyl 3-deoxy-4,5:7,8-di*-O-*isopropylidene*-α,β-D-manno-*2-octulopyranosonate* **6**

A solution of **5** (30 mg, 64 μmol) in dry and degassed toluene (2 mL) was treated with Bu_3SnH (32 μL, 0.12 mmol) and AIBN (0.2 mg) under argon atmosphere. The mixture was heated at 90°C for 2 h, then stirred for 2 h at room temperature and evaporated to dryness. Flash chromatography of the residue (toluene:EtOAc, 3:1) gave **6** (18 mg, 83%) as a colourless syrup. The physical data were in full accordance with those reported.[2a,10a]

3.7. *Methyl 3*-O-*acetyl-4,5:7,8-di*-O-*isopropylidene*-α-D-glycero-D-galacto-*2-octulopyranosonate* **7**

A solution of **3** (2.30 g, 4.91 mmol) in 98% acetone (200 mL) was treated with NIS (2.76 g, 12.28 mmol) at 0°C. The solution turned red; after 30 min (monitored by TLC) the reaction was stopped with NEt_3 (20 mL) and evaporated in vacuo to dryness. The residue was dissolved in CH_2Cl_2:pyridine (10:1, 70 mL) and treated with AcCl (0.60 mL, 8.35 mmol). After 3 h the mixture was diluted with EtOAc, then washed with satd. aqueous $NaHCO_3$ and satd. aqueous $Na_2S_2O_3$. The organic phase was dried ($MgSO_4$) and concentrated. Flash chromatography of the residue (toluene:acetone, 3:1) afforded **7** (1.30 g, 70%); TLC (toluene:EtOAc, 1:1): R_f 0.33; $[\alpha]_D$ +72.7 (*c* 1, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.35, 1.38, 1.41, 1.57 [4s, 12H, C(CH_3)$_2$], 2.05 (s, 3H, $COCH_3$), 3.81 (s, 3H, $COOCH_3$), 3.95 (dd, 1H, $J_{7,8}$=4.7 Hz, $J_{8,8'}$=8.9 Hz, 8-H), 4.04 (dd, 1H, $J_{7,8'}$=6.1 Hz, 8′-H), 4.14 (dd, 1H, $J_{5,6}$=2.5 Hz, $J_{6,7}$=8.2 Hz, 6-H), 4.18 (d, 1H, $J_{3,OH}$=< 1 Hz, OH), 4.31 (dd, 1H, $J_{3,4}$=7.4 Hz, $J_{4,5}$=5.2 Hz, 4-H), 4.32 (dd, 1H, 5-H), 4.38 (ddd, 1H, 7-H), 5.32 (dd, 1H, 3-H); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ: 20.8–27.7 [5C, C(*C*H_3)$_2$, CO*C*H_3], 53.9 (1C, COO*C*H_3), 66.9 (1C, 8-C), 70.0 (1C, 6-C), 71.1 (1C, 3-C), 73.1 (1C, 5-C), 73.9 (1C, 7-C), 74.7 (1C, 4-C), 94.1 (1C, 2-C), 109.5, 110.1 [2C, *C*(CH_3)$_2$], 169.3, 169.6 (2C, *C*OCH_3, *C*$OOCH_3$). Anal. calcd for $C_{17}H_{26}O_{10}$ (390.39): C, 52.30; H, 6.71; found: C, 52.19; H, 6.74.

3.8. *Methyl 2*-O-*allyl-4,5:7,8-di*-O-*isopropylidene*-α-D-glycero-D-galacto-*2-octulopyranosonate* ***8***

NaH (50 mg, 2.10 mmol) was slowly added to a solution of **7** (550 mg, 1.41 mmol) and AllBr (143 μL, 1.70 mmol) in dry DMF (15 mL). After 12 h at room temperature, the reaction mixture was treated with dry MeOH (10 mL) and stirred for a further 6 h. After the usual workup (NH_4Cl, EtOAc), the organic layer was dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (toluene:EtOAc, 3:1) gave **8** (395 mg, 72%) as a colourless syrup; TLC (toluene:EtOAc, 1:1): R_f 0.45; $[\alpha]_D$ +7.1 (*c* 0.25, $CHCl_3$); ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.25, 1.26, 1.30, 1.35 [4s, 12H, C$(CH_3)_2$], 3.66 (s, 3H, $COOCH_3$), 3.80 (dd, 1H, $J_{5,6}$=2.3 Hz, $J_{6,7}$=7.9 Hz, 6-H), 3.86 (dd, 1H, $J_{7,8}$=5 Hz, $J_{8,8'}$=8.5 Hz, 8-H), 3.89 (dd, 1H, $J_{3,4}$=7.0 Hz, $J_{3,OH}$=6.7 Hz, 3-H), 3.98–4.11 (m, 3H, 8′-H, CH_2CH=CH_2), 4.18–4.21 (m, 2H, 4-, 7-H), 4.25 (dd, 1H, $J_{4,5}$=6.2 Hz, 5-H), 5.13 (dd, 1H, J_{vic}=10.6 Hz, J_{gem}=1 Hz, CH_2CH=CH_2), 5.30 (dd, 1H, J_{vic}=17.3 Hz, CH_2CH=CH_2), 5.54 (d, 1H, OH), 5.90 (m, 1H, CH_2CH=CH_2); ^{13}C NMR (150.9 MHz, DMSO-d_6) δ: 25.3, 25.8, 26.6, 27.0 [4C, C(CH_3)$_2$], 52.2 (1C, COOCH_3), 63.5 (1C, CH_2CH=CH_2), 66.0 (1C, 8-C), 69.6 (1C, 3-C), 70.2 (1C, 6-C), 72.0 (1C, 5-C), 73.4 (1C, 7-C), 75.0 (1C, 4-C), 98.1 (1C, 2-C), 108.4, 108.6 [2C, $C(CH_3)_2$], 116.4 (1C, CH_2CH=CH_2), 134.4 (1C, CH_2CH=CH_2), 167.9 (1C, 1-C); MALDI-MS: $[M+Na]^+$=411, $[M+K]^+$=427. Anal. calcd for $C_{18}H_{28}O_9$ (388.41): C, 55.66; H, 7.27; found: C, 55.55; H, 7.19.

3.9. *Methyl 2*-O-*allyl-4,5:7,8-di*-O-*isopropylidene*-α-D-glycero-D-talo-*2-octulopyranosonate* ***9***

A solution of **8** (1.30 g, 3.35 mmol) in CH_2Cl_2 (30 mL) was treated with Dess–Martin periodinane (2.84 g, 6.70 mmol) and stirred for 2 h. The homogeneous mixture was diluted with Et_2O (300 mL) and satd. aqueous $NaHCO_3$ (100 mL) containing $Na_2S_2O_3$ (10 g). After stirring for 1 h, the organic layer was separated, washed with satd. aqueous $NaHCO_3$ (100 mL) and dried ($MgSO_4$). Removal of the solvent afforded the ketone as a colourless syrup, R_f=0.65 (toluene:EtOAc, 1:1). The ketone was dissolved in dry MeOH (30 mL) and stirred with BH_3–NH_3 (140 mg, 4.09 mmol) for 30 min at 0°C. The residue obtained upon evaporation was purified by flash chromatography (toluene:EtOAc, 3:1) to yield **9** (1.13 g, 87%) and **8** (0.05 g, 4%) as colourless syrups; TLC (toluene:EtOAc, 1:1): R_f 0.38; $[\alpha]_D$ +7.9 (*c* 0.25, $CHCl_3$); ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.24, 1.27, 1.32, 1.40 [4s, 12H, C$(CH_3)_2$], 3.63 (s, 3H, $COOCH_3$), 3.65 (dd, 1H, $J_{5,6}$=2.3 Hz, $J_{6,7}$=6.7 Hz, 6-H), 3.76 (dd, 1H, J_{gem}=13 Hz, J_{vic}=5.3 Hz, CH_2CH=CH_2), 3.78 (dd, 1H, $J_{3,4}$=4.1 Hz, $J_{3,OH}$=6.5 Hz, 3-H), 3.90 (dd, 1H, $J_{7,8}$=5.6 Hz, $J_{8,8'}$=8.6 Hz, 8-H), 3.97 (dd, 1H, J_{vic}=5.3 Hz, CH_2CH=CH_2), 4.00 (dd, 1H, $J_{7,8'}$=6.5 Hz, 8′-H), 4.20–4.29 (m, 2H, 5-, 7-H), 4.30 (dd, 1H, $J_{4,5}$=7 Hz, 4-H), 5.13 (dd, 1H, J_{vic}=10.3 Hz, J_{gem}=1.5 Hz, CH_2CH=CH_2), 5.26 (dd, 1H, J_{vic}=17 Hz, CH_2CH=CH_2), 5.33 (d, 1H, OH), 5.86 (m, 1H, CH_2CH=CH_2); ^{13}C NMR (150.9 MHz, DMSO-d_6) δ: 25.3, 25.4, 26.5 [4C, C(CH_3)$_2$], 51.8 (1C, COOCH_3), 63.5 (1C, CH_2CH=CH_2), 65.7 (1C, 8-C), 67.9 (1C, 3-C), 79.3 (1C, 6-C), 71.1 (1C, 5-C), 72.8 (1C, 4-C), 73.6 (1C, 7-C), 100.8 (1C, 2-C), 108.2, 108.8 [2C, $C(CH_3)_2$], 116.6 (1C, CH_2CH=CH_2), 134.1 (1C, CH_2CH=CH_2), 167.1 (1C, 1-C); MALDI-MS: $[M+Na]^+$=411, $[M+K]^+$=427. Anal. calcd for $C_{18}H_{28}O_9$ (388.41): C, 55.66; H, 7.27; found: C, 55.53; H, 7.24.

3.10. *Methyl 2*-O-*allyl-3*-O-*benzoyl-4,5:7,8-di*-O-*isopropylidene*-α-D-glycero-D-talo-*2-octulopyranosonate* ***10***

A solution of **9** (300 mg, 0.77 mmol) in dry CH_2Cl_2 (10 mL) was treated with DMAP (376 mg, 3.08 mmol) and benzoyl chloride (0.18 mL, 1.54 mmol), and stirred for 24 h at room temperature. After usual workup ($NaHCO_3$, EtOAc), the organic layer was dried ($MgSO_4$) and concentrated in

vacuo. Flash chromatography (toluene:EtOAc, 5:1) gave **10** (348 mg, 92%) as a colourless syrup; TLC (toluene:EtOAc, 1:1): R_f 0.75; $[\alpha]_D$ +73.5 (*c* 1, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.22, 1.29, 1.39, 1.47 [4s, 12H, $C(CH_3)_2$], 3.63 (s, 3H, $COOCH_3$), 3.90–4.58 (m, 7H, 5-, 6-, 7-, 8-, 8′-H, $CH_2CH{=}CH_2$), 4.65 (dd, 1H, $J_{3,4}$=5.0 Hz, $J_{4,5}$=6.3 Hz, 4-H), 5.15–5.32 (m, 2H, $CH_2CH{=}CH_2$), 5.50 (d, 1H, 3-H), 5.88 (m, 1H, $CH_2CH{=}CH_2$), 7.38–8.02 (m, 5H, Ph). Anal. calcd for $C_{25}H_{32}O_{10}\cdot\frac{1}{4}H_2O$ (497.02): C, 60.41; H, 6.59; found: C, 60.38; H, 6.58.

3.11. Methyl 2-deoxy-2-ethylthio-4,5:7,8-di-O-*isopropylidene-α,β*-D-glycero-D-galacto-*2-octulopyranosonate* ***11***

A solution of **3** (6.80 g, 15.0 mmol) in dry CH_3CN:CH_2Cl_2 (10:1, 150 mL) was cooled to −30°C and treated with NIS (3.54 g, 15.7 mmol). After 30 min, the reaction was stopped with NEt_3 (10 mL). The mixture was diluted with EtOAc, washed with satd. aqueous $NaHCO_3$ (100 mL) containing $Na_2S_2O_3$ (10 g), and then with water. The organic phase was dried ($MgSO_4$) and concentrated. Flash chromatography (toluene:EtOAc, 5:1) of the residue afforded **11α** (4.53 g, 77%) as a solid. Further elution of the column gave **11β** (0.47 g, 8%) as a colourless syrup; **α**: TLC (toluene:EtOAc, 1:1): R_f 0.53; m.p. 167°C; $[\alpha]_D$ +108.6 (*c* 1, $CHCl_3$); ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.10 (t, 3H, *J*=7.5 Hz, SCH_2CH_3), 1.22, 1.25, 1.26, 1.31 [4s, 12H, $C(CH_3)_2$], 2.37–2.50 (m, 2H, SCH_2CH_3), 3.64 (s, 3H, $COOCH_3$), 3.74 (dd, 1H, $J_{7,8}$=4.9 Hz, $J_{8,8'}$=8.3 Hz, 8-H), 3.90 (dd, 1H, $J_{5,6}$=1.7 Hz, $J_{6,7}$=8.0 Hz, 6-H), 4.00 (dd, 1H, $J_{7,8'}$=6.4 Hz, 8′-H), 4.10 (ddd, 1H, 7-H), 4.25 (dd, 1H, $J_{4,5}$=7.6 Hz, 5-H), 4.37 (dd, 1H, $J_{3,4}$=3.7 Hz, 4-H), 4.46 (dd, 1H, $J_{3,OH}$=6.7 Hz, 3-H), 6.28 (d, 1H, OH); ^{13}C NMR (150.9 MHz, DMSO-d_6) δ: 14.3 (1C, SCH_2CH_3), 20.9 (1C, SCH_2CH_3), 24.9, 25.0, 25.2, 26.6 [4C, $C(CH_3)_2$], 52.1 (1C, $COOCH_3$), 66.2 (1C, 8-C), 67.1 (1C, 3-C), 70.4 (1C, 6-C), 71.7 (1C, 5-C), 72.7 (1C, 7-C), 73.9 (1C, 4-C), 90.0 (1C, 2-C), 108.3, 109.5 [2C, $C(CH_3)_2$], 169.6 (1C, 1-C). Anal. calcd for $C_{17}H_{28}O_8S$ (392.46): C, 52.03; H, 7.19; found: C, 51.75; H, 7.15. **β**: TLC (toluene:EtOAc, 1:1): R_f 0.47; $[\alpha]_D$ +10.1 (*c* 0.5, $CHCl_3$); ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.07 (t, 3H, *J*=7.5 Hz, SCH_2CH_3), 1.25, 1.26, 1.30, 1.44 [4s, 12H, $C(CH_3)_2$], 2.37–2.52 (m, 2H, SCH_2CH_3), 3.67 (s, 3H, $COOCH_3$), 3.69 (dd, 1H, $J_{5,6}$=1.6 Hz, $J_{6,7}$=8.7 Hz, 6-H), 3.99 (dd, 1H, $J_{3,4}$=3.4 Hz, $J_{3,OH}$=6.6 Hz, 3-H), 4.00 (dd, 1H, $J_{7,8}$=6.4 Hz, $J_{8,8'}$=8.2 Hz, 8-H), 4.07 (dd, 1H, $J_{7,8'}$=4.2 Hz, 7-H), 4.21 (dd, 1H, 8′-H), 4.27 (dd, 1H, $J_{4,5}$=7.8 Hz, 5-H), 4.35 (dd, 1H, 4-H), 6.19 (d, 1H, OH); ^{13}C NMR (150.9 MHz, DMSO-d_6) δ: 14.6 (1C, SCH_2CH_3), 23.7 (1C, SCH_2CH_3), 24.7, 25.0, 25.7, 26.7 [4C, $C(CH_3)_2$], 52.1 (1C, $COOCH_3$), 66.2 (1C, 8-C), 68.1 (1C, 3-C), 70.7 (1C, 5-C), 72.4 (1C, 6-C), 72.9 (1C, 7-C), 74.0 (1C, 4-C), 88.1 (1C, 2-C), 108.5, 109.4 [2C, $C(CH_3)_2$], 169.4 (1C, 1-C). Anal. calcd for $C_{17}H_{28}O_8S$ (392.46): C, 52.03; H, 7.19; found: C, 52.03; H, 7.17.

3.12. Methyl 2-deoxy-2-ethylthio-4,5:7,8-di-O-*isopropylidene-α*-D-glycero-D-talo-*2-octulopyranosonate* ***12***

A solution of **11α** (2.70 g, 6.88 mmol) in CH_2Cl_2 (40 mL) was treated with Dess–Martin periodinane (4.38 g, 10.33 mmol) and stirred for 2 h. The homogeneous mixture was diluted with Et_2O (350 mL) and satd. aqueous $NaHCO_3$ (100 mL) containing $Na_2S_2O_3$ (10 g), and stirred for 1 h. The organic layer was separated, washed with satd. aqueous $NaHCO_3$ (100 mL) and dried ($MgSO_4$). Removal of the solvent without further purification gave the ketone as a colourless syrup, R_f=0.77 (toluene:EtOAc, 1:1). A solution of the ketone in dry MeOH (50 mL) was stirred with BH_3–NH_3 (288 mg, 8.41 mmol) for 30 min at 0°C. The residue obtained upon evaporation was purified by flash chromatography (toluene:EtOAc, 3:1) to afford **12** (2.38 g, 88%) and **11α** (0.11 g, 4%) as a colourless syrup and a solid, respectively. Data for **12**: TLC (toluene:EtOAc, 1:1): R_f 0.58; $[\alpha]_D$ +111.7 (*c* 1, $CHCl_3$); ^{1}H NMR (250 MHz, DMSO-

d_6) δ: 1.11 (t, 3H, J=7.5 Hz, SCH_2CH_3), 1.24, 1.27, 1.35, 1.37 [4s, 12H, $C(CH_3)_2$], 2.43–2.50 (m, 2H, SCH_2CH_3), 3.67 (s, 3H, $COOCH_3$), 3.85–4.03 (m, 4H, 3-, 6-, 8-, 8′-H), 4.22–4.30 (m, 3H, 4-, 5-, 7-H), 5.27 (d, 1H, $J_{3,OH}$=7.4 Hz, OH); MALDI-MS: $[M+Na]^+$=415, $[M+K]^+$=431. Anal. calcd for $C_{17}H_{28}O_8S$ (392.46): C, 52.03; H, 7.19; found: C, 51.99; H, 7.18.

*3.13. Methyl 3-*O*-benzoyl-2-deoxy-2-ethylthio-4,5:7,8-di-*O*-isopropylidene-α-*D*-glycero-*D*-talo-2-octulopyranosonate **13***

A solution of **12** (1.50 g, 3.83 mmol) in dry CH_2Cl_2 (30 mL) was treated with DMAP (1.20 g, 9.84 mmol) and benzoyl chloride (0.66 mL, 5.74 mmol), and stirred for 24 h at room temperature. After the usual workup ($NaHCO_3$, EtOAc), the organic layer was dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (toluene:EtOAc, 8:1) gave **13** (1.82 g, 96%) as a colourless syrup; TLC (toluene:EtOAc, 1:1): R_f 0.79; $[\alpha]_D$ +109.4 (*c* 1, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.11, 1.27, 1.40, 1.51 [4s, 12H, $C(CH_3)_2$], 1.21 (t, 3H, J=7.5 Hz, SCH_2CH_3), 2.52–2.58 (m, 2H, SCH_2CH_3), 3.56 (s, 3H, $COOCH_3$), 4.17 (dd, 1H, $J_{7,8}$=6.3 Hz, $J_{8,8'}$=8.9 Hz, 8-H), 4.25 (dd, 1H, $J_{7,8'}$=4.9 Hz, 8′-H), 4.30 (dd, 1H, $J_{4,5}$=5.9 Hz, $J_{5,6}$=2.8 Hz, 5-H), 4.35 (dd, 1H, $J_{6,7}$=6.1 Hz, 6-H), 4.54 (ddd, 1H, 7-H), 4.61 (dd, 1H, $J_{3,4}$=5.4 Hz, 4-H), 5.58 (d, 1H, 3-H), 7.37–8.02 (m, 5H, Ph); MALDI-MS: $[M+Na]^+$=519, $[M+K]^+$=535. Anal. calcd for $C_{24}H_{32}O_9S$ (496.57): C, 58.05; H, 6.49; found: C, 58.15; H, 6.29.

*3.14. Methyl 3-*O*-benzoyl-4,5:7,8-di-*O*-isopropylidene-α,β-*D*-glycero-*D*-talo-2-octulopyranosonate **14***

I. From **10**: A solution of **10** (100 mg, 203 μmol) in dry THF (5 mL) was treated with anhydrous $ZnCl_2$ (68 mg, 508 μmol). After 15 min at room temperature, $Pd(PPh_3)_4$ (39 mg, 34 μmol) was added to the reaction mixture and stirred for 10 min protected from light. Then Bu_3SnH (267 μL, 1.01 mmol) was added and the reaction mixture was stirred overnight. After the usual workup (Et_2O, H_2O), the organic layer was dried ($MgSO_4$) and concentrated in vacuo to dryness. The residue was dissolved in 2-methoxypropene (3 mL), treated with *p*-toluenesulfonic acid (1 mg), and the reaction mixture was stirred for 3 h at room temperature. After the usual workup ($NaHCO_3$, EtOAc), the organic layer was dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (toluene:EtOAc, 3:1) gave **14** (40 mg, 43%) as a white foam.

II. From **13**: NIS (3.54 g, 15.7 mmol) and AcOH (73 μL, 1.21 mmol) were added to a solution of **13** (6.00 g, 12.1 mmol) in 99% acetone (100 mL). The mixture was cooled to 15°C and treated with trifluoromethanesulfonic acid (4 μL, 0.02 mmol). The mixture was stirred for 20 min and then neutralised with NEt_3. After the usual workup ($NaHCO_3$, EtOAc), the organic layer was dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (toluene:EtOAc, 8:1→3:1) afforded **14** (3.87 g, 70%) and educt **13** (1.44 g, 24%). Data for **14**: TLC (toluene:EtOAc, 1:1): R_f 0.51–0.66; **α**: ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.07, 1.20, 1.29, 1.38 [4s, 12H, $C(CH_3)_2$], 3.50 (s, 3H, $COOCH_3$), 4.02–4.11 (m, 3H, 8-, 8′-, 6-H), 4.31 (dd, 1H, $J_{4,5}$=6.0 Hz, $J_{5,6}$=3.0 Hz, 5-H), 4.34 (ddd, 1H, $J_{6,7}$=7.3 Hz, $J_{7,8}$=5.3 Hz, $J_{7,8'}$=5.3 Hz, 7-H), 4.58 (dd, 1H, $J_{3,4}$=5.4 Hz, 4-H), 5.29 (d, 1H, 3-H), 7.53–7.88 (m, 6H, OH, Ph); ^{13}C NMR (150.9 MHz, DMSO-d_6) δ: 25.3, 25.4, 26.6 [4C, $C(CH_3)_2$], 52.0 (1C, $COOCH_3$), 65.6 (1C, 8-C), 67.6 (1C, 3-C), 68.2 (1C, 6-C), 69.4 (1C, 5-C), 69.5 (1C, 4-C), 73.4 (1C, 7-C), 95.0 (1C, 2-C), 108.5, 108.6 [2C, $C(CH_3)_2$], 128.7–133.7 (6C, Ph), 164.3 (1C, *C*OPh), 168.3 (1C, 1-C); **β**: ^{1}H NMR (600 MHz, DMSO-d_6) δ: 1.26, 1.35, 1.38, [3s, 12H, $C(CH_3)_2$], 3.67 (s, 3H, $COOCH_3$), 3.81 (dd, 1H, $J_{5,6}$=2.3 Hz, $J_{6,7}$=7.8 Hz, 6-H), 3.90 (dd, 1H, $J_{7,8}$=4.7 Hz, $J_{8,8'}$=8.5 Hz, 8-H), 4.02 (dd, 1H, $J_{7,8'}$=6.2 Hz, 8′-H), 4.16 (ddd, 1H, 7-H), 4.45 (dd, 1H, $J_{4,5}$=7.9 Hz, 5-H), 4.70 (dd, 1H, $J_{3,4}$=3.5 Hz, 4-H), 5.54 (d, 1H, 3-H), 6.59 (s, 1H, OH), 7.52–8.00 (m, 5H, Ph); ^{13}C NMR (150.4 MHz, DMSO-d_6) δ: 24.7, 25.1, 25.4, 26.6 [4C,

C(CH_3)$_2$], 52.2 (1C, COOCH_3), 65.9 (1C, 8-C), 67.4 (1C, 3-C), 71.6 (2C, 4-, 6-C), 71.6 (1C, 5-C), 72.8 (1C, 7-C), 95.3 (1C, 2-C), 108.5, 109.5 [2C, C(CH_3)$_2$], 128.7–133.7 (6C, Ph), 165.1 (1C, COPh), 164.3 (1C, 1-C); MALDI-MS: $[M+Na]^+$=475, $[M+K]^+$=491. Anal. calcd for $C_{22}H_{28}O_{10}\cdot\frac{1}{4}H_2O$ (456.96): C, 57.82; H, 6.29; found: C, 58.02; H, 6.31.

*3.15. Methyl 3-*O*-benzoyl-2-*O*-diethylphosphite-4,5:7,8-di-*O*-isopropylidene-α,β-*D*-glycero-*D*-talo-2-octulopyranosonate* ***15***

Hünig's base (6.46 mL, 3.78 mmol) and diethyl chlorophosphite (420 μl, 2.94 mmol) were added to a solution of **14** (960 mg, 2.10 mmol) in dry acetonitrile (30 mL) at room temperature. After 1 h, the solution was treated with NEt_3 (3 mL) and satd. aqueous $NaHCO_3$, and extracted with EtOAc. The organic layer was dried ($MgSO_4$), concentrated in vacuo and purified by flash chromatography (toluene:NEt_3, 100:1) to afford **15** (1.09 g, 91%) as a white foam; TLC (toluene:EtOAc, 1:1, +1% NEt_3): R_f 0.73–0.78; ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.16–1.54 [m, 18H, C(CH_3)$_2$, OCH$_2$CH_3], 3.66, 3.78 (2s, 3H, COOCH_3), 3.78–4.26 (m, 7H, OCH_2CH$_3$, 8-, 8′-, 7-H), 4.30–4.53 (m, 2H, 5-, 6-H), 4.65–4.75 (2 dd, 1H, 4α-, 4β-H), 5.48–5.50 (2 d, 1H, 3α-, 3β-H), 7.38–8.16 (m, 5H, Ph); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ: 16.7 (2C, OCH$_2$CH_3), 24.6–27.1 [4C, C(CH_3)$_2$], 52.5, 52.8 (1C, COOCH_3), 58.3–58.8 (2C, OCH_2CH$_3$), 66.6, 66.8 (1C, 8-C), 67.7, 69.2 (1C, 3-C), 70.4, 71.6 (1C, 4-C), 70.6, 72.1 (1C, 5-C), 73.1 (1C, 7-C), 73.4, 73.7 (1C, 6-C), 109.4, 109.6 [2C, C(CH_3)$_2$], 110.3, 110.8 (1C, 2-C), 125.3–133.4 (6C, Ph), 165.3, 165.9 (1C, COPh), 166.8, 169.0 (1C, 1-C). Anal. calcd for $C_{26}H_{37}O_{12}P$ (572.54): C, 54.54; H, 6.51; found: C, 54.53; H, 6.39.

3.16. Methyl O*-(methyl 3-*O*-benzoyl-4,5:7,8-di-*O*-isopropylidene-α-*D*-glycero-*D*-talo-2-octulopyranosonate)-(2→6)-2,3,4-tri-*O*-benzyl-α-*D*-glucopyranoside* ***18*** *and methyl 2,6-anhydro-3-*O*-benzoyl-2-deoxy-4,5:7,8-di-*O*-isopropylidene-*D*-manno-oct-2-enosonate* ***17***

A solution of **16** (568 mg, 1.22 mmol) and donor **15** (942 mg, 1.65 mmol) in dry CH_2Cl_2 (10 mL) was cooled to −20°C under argon atmosphere. Then TMSOTf (120 μL, 0.66 mmol) was added to the solution. After 3 h at −15°C, the reaction was allowed to reach room temperature (5 min), neutralised with NEt_3 (3 mL) and concentrated. Flash chromatography (toluene:EtOAc, 10:1) of the residue afforded **18** (680 mg, 62%) and **17** (290 mg, 40%) as white foams; **18**: TLC (toluene:EtOAc, 1:1): R_f 0.76; $[\alpha]_D$ +24.6 (*c* 0.5, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.16, 1.22, 1.31, 1.32 [4s, 12H, C(CH_3)$_2$], 3.16 (dd, 1H, $J_{3a,4a}$=9.1 Hz, $J_{4a,5a}$=9.8 Hz, 4a-H), 3.25 (s, 3H, OCH_3), 3.40–3.46 (m, 5H, 2a-, 6a-H, COOCH_3), 3.54 (dd, 1H, $J_{6a,6'a}$=10.6 Hz, $J_{5a,6'a}$=1 Hz, 6′a-H), 3.72 (ddd, 1H, $J_{5a,6a}$=9.0 Hz, 5a-H), 3.89 (dd, 1H, $J_{2a,3a}$=9.2 Hz, 3a-H), 3.93 (dd, 1H, $J_{5b,6b}$=2.8 Hz, $J_{6b,7b}$=7.5 Hz, 6b-H), 4.06–4.10 (m, 2H, 8b-, 8′b-H), 4.21 (dd, 1H, $J_{4b,5b}$=6.6 Hz, 5b-H), 4.38–4.92 (m, 9H, 7b-, 1a-, 4b-H, CH_2Ph), 5.40 (d, 1H, $J_{3b,4b}$=5.0 Hz, 3b-H), 7.12–7.95 (m, 20H, Ph); MALDI-MS: $[M+Na]^+$=922, $[M+K]^+$=938. Anal. calcd for $C_{50}H_{58}O_{15}$ (899.00): C, 66.80; H, 6.50; found: C, 66.60; H, 6.41. **17**: TLC (toluene:EtOAc, 1:1, +1% NEt_3): R_f 0.65; $[\alpha]_D$ +20.4 (*c* 0.25, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.38, 1.40, 1.44, 1.50 [4s, 12H, C(CH_3)$_2$], 3.66 (s, 3H, COOCH_3), 3.93 (dd, 1H, $J_{5,6}$=1.1 Hz, $J_{6,7}$=8.5 Hz, 6-H), 4.17–4.20 (m, 2H, 8-, 8′-H), 4.47 (ddd, 1H, $J_{7,8}$=4.3 Hz, $J_{7,8'}$=5.7 Hz, 7-H), 4.63 (dd, 1H, $J_{4,5}$=6.7 Hz, 5-H), 4.93 (d, 1H, 4-H), 7.42–8.13 (m, 5H, Ph). Anal. calcd for $C_{22}H_{26}O_9$ (434.44): C, 60.82; H, 6.03; found: C, 60.88; H, 6.12.

3.17. *Methyl* O-*(methyl 4,5:7,8-di*-O-*isopropylidene-α*-D-glycero-D-talo-*2-octulopyranosonate)-(2→6)-2,3,4-tri*-O-*benzyl-α*-D-*glucopyranoside* ***19***

A solution of **18** (650 mg, 0.72 mmol) in dry MeOH (10 mL) was treated with 1 M MeONa in MeOH (0.5 mL) and stirred for 24 h at 30°C. The reaction mixture was neutralised with satd. aqueous NH_4Cl and extracted with EtOAc. Then the organic layer was dried ($MgSO_4$), concentrated in vacuo and the residue was purified by flash chromatography (toluene:EtOAc, 4:1) to give **19** (517 mg, 90%) as a colourless foam; TLC (toluene:EtOAc, 1:1): R_f 0.49; $[\alpha]_D$ +47.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.32, 1.36, 1.38, 1.51 [4s, 12H, $C(CH_3)_2$], 2.88 (d, 1H, $J_{3b,OH}$=8.3 Hz, OH), 3.24 (dd, 1H, $J_{3a,4a}$=9.2 Hz, $J_{4a,5a}$=9.8 Hz, 4a-H), 3.34 (s, 3H, OCH_3), 3.47–3.51 (m, 2H, 2a-, 6a-H), 3.60 (dd, 1H, $J_{6a,6'a}$=9.0 Hz, $J_{5a,6'a}$=1 Hz, 6′a-H), 3.68 (s, 3H, $COOCH_3$), 3.78 (ddd, 1H, $J_{5a,6a}$=9.5 Hz, 5a-H), 3.87 (dd, 1H, $J_{5b,6b}$=2.5 Hz, $J_{6b,7b}$=8.2 Hz, 6b-H), 3.91 (dd, 1H, $J_{3b,4b}$=4.1 Hz, 3b-H), 3.97 (dd, 1H, $J_{2a,3a}$=9.2 Hz, 3a-H), 4.05 (dd, 1H, $J_{8b,8'b}$=8.5 Hz, $J_{7b,8b}$=4.5 Hz, 8b-H), 4.10 (dd, 1H, $J_{7b,8'b}$=6.0 Hz, 8′b-H), 4.26 (dd, 1H, $J_{4b,5b}$=6.2 Hz, 5b-H), 4.36 (dd, 1H, 4b-H), 4.40 (ddd, 1H, 7b-H), 4.50–4.98 (m, 7H, 1a-H, CH_2Ph), 7.14–7.39 (m, 15H, Ph); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ: 25.3–26.8 [4C, C(*C*H_3)$_2$], 52.5 (1C, COO*C*H_3), 54.8 (1C, OCH_3), 63.8 (1C, 6a-C), 66.9 (1C, 8b-C), 68.5 (1C, 3b-C), 69.3 (1C, 5a-C), 69.5 (1C, 6b-C), 71.3 (1C, 5b-C), 72.3 (1C, 4b-C), 73.7 (1C, 7b-C), 73.4, 74.8, 75.7 (3C, CH_2Ph), 78.3 (1C, 4a-C), 79.9 (1C, 2a-C), 82.0 (1C, 3a-C), 97.6 (1C, 1a-C), 99.3 (1C, 2b-C), 109.3, 109.8 [2C, *C*$(CH_3)_2$], 127.6–138.6 (18C, Ph), 167.6 (1C, 1b-C). Anal. calcd for $C_{43}H_{54}O_{14}$ (794.89): C, 64.97; H, 6.85; found: C, 64.66; H, 6.61.

3.18. *Methyl* O-*(methyl 4,5:7,8-di*-O-*isopropylidene-3*-O-*thiobenzoyl-α*-D-glycero-D-talo-*2-octulo-pyranosonate)-(2→6)-2,3,4-tri*-O-*benzyl-α*-D-*glucopyranoside* ***20***

N,*N*-Dimethyl-α-chlorobenzimidium chloride (186 mg, 910 μmol) was added to a solution of **19** (290 mg, 360 μmol) in dry CH_2Cl_2:pyridine (10:1, 5 mL). After 24 h at room temperature, the reddish solution was treated with H_2S. Then satd. aqueous $NaHCO_3$ was added and the mixture was extracted with EtOAc. The organic layer was dried ($MgSO_4$), concentrated in vacuo and the residue was purified by flash chromatography (toluene:EtOAc, 15:1) to give **20** (314 mg, 94%) as a yellow syrup; TLC (toluene:EtOAc, 1:1): R_f 0.81; $[\alpha]_D$ +4.0 (*c* 1, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.18, 1.27, 1.37, 1.38 [4s, 12H, $C(CH_3)_2$], 3.30 (s, 3H, OCH_3), 3.45–3.62 (m, 6H, 2a-, 6a-, 6′a-H, $COOCH_3$), 3.79 (ddd, 1H, $J_{5a,6a}$=7.9 Hz, $J_{5a,6'a}$=1.6 Hz, 5a-H), 3.96 (dd, 1H, $J_{2a,3a}$=9.1 Hz, 3a-H), 4.03 (dd, 1H, $J_{5b,6b}$=2.7 Hz, $J_{6b,7b}$=7.3 Hz, 6b-H), 4.12–4.98 (m, 12H, 8b-, 8′b-, 5b-, 7b-, 1a-, 4b-H, CH_2Ph), 6.27 (d, 1H, $J_{3b,4b}$=4.8 Hz, 3b-H), 7.15–8.12 (m, 20H, Ph). Anal. calcd for $C_{50}H_{58}O_{14}S\cdot H_2O$ (933.08): C, 64.36; H, 6.48; found: C, 64.31; H, 6.58.

3.19. *Methyl* O-*(methyl 3-deoxy-4,5:7,8-di*-O-*isopropylidene-α*-D-manno-*2-octulopyranosonate)-(2→6)-2,3,4-tri*-O-*benzyl-α*-D-*glucopyranoside* ***21***

A solution of **20** (50 mg, 54 μmol) in dry and degassed toluene (2 mL) was treated with Bu_3SnH (43 μL, 0.16 mmol) and AIBN (0.2 mg) under argon atmosphere. The mixture was heated at 90°C for 2 h, then stirred 2 h at room temperature and evaporated to dryness. Flash chromatography of the residue (toluene:EtOAc, 3:1) gave **21** (32 mg, 76%). The physical data were in full accordance with those reported.[20]

*3.20. Thexyldimethylsilyl 2-azido-3,4-di-*O*-benzyl-2-deoxy-β-*D*-glucopyranoside **22***

A mixture of thexyldimethylsilyl 2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside[22] (1.14 g, 2.16 mmol) and 1 M BH_3 in THF (25 mL) was cooled to 0°C and treated with TMSOTf (195 μl, 1.08 mmol) dissolved in 1 mL of dry CH_2Cl_2. After 18 h at 0°C, NEt_3 (3 mL) was added to the reaction mixture followed by careful addition of MeOH until the evolution of H_2 had ceased. The reaction mixture was co-distilled with MeOH three times before being purified by flash chromatography (petroleum ether:EtOAc, 9:1) to give **22** (0.95 g, 83%) as a colourless oil; TLC (toluene): R_f 0.42; $[\alpha]_D$ −31.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 0.19, 0.20 [2s, 6H, $Si(CH_3)_2$], 0.89–0.91 [m, 12H, $SiC(CH_3)_2CH(CH_3)_2$], 1.64–1.69 [m, 1H, $SiC(CH_3)_2CH(CH_3)_2$], 1.81 (dd, 1H, $J_{6,OH}$=7.7 Hz, $J_{6',OH}$=5.9 Hz, OH), 3.30 (dd, 1H, $J_{1,2}$=7.9 Hz, $J_{2,3}$=10 Hz, 2-H), 3.34 (ddd, 1H, $J_{4,5}$=9.6 Hz, $J_{5,6}$=4.7 Hz, $J_{5,6'}$=2.7 Hz, 5-H), 3.42 (dd, 1H, $J_{3,4}$=9.4 Hz, 3-H), 3.55 (dd, 1H, 4-H), 3.68 (ddd, 1H, $J_{6,6'}$=12 Hz, 6-H), 3.82 (ddd, 1H, 6′-H), 4.54 (d, 1H, 1-H), 4.54–4.90 (m, 4H, CH_2Ph), 7.25–7.39 (m, 10H, Ph); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ: −3.2, −2.0 [2C, $Si(CH_3)_2$], 18.4–33.9 [6C, $SiC(CH_3)_2CH(CH_3)_2$], 62.0 (1C, 6-C), 68.9 (1C, 2-C), 75.0–75.5 (3C, 5-C, CH_2Ph), 77.5 (1C, 4-C), 82.9 (1C, 3-C), 96.9 (1C, 1-C), 127.8–138.0 (12C, Ph); FAB-MS (nominal mass): MH^+=528, $[M+Na]^+$=550, $[M+NaI]Na^+$=700. Anal. calcd for $C_{28}H_{41}N_3O_5Si$ (527.73): C, 63.73; H, 7.83; N, 7.96; found: C, 63.99; H, 7.73; N, 8.06.

3.21. Thexyldimethylsilyl O-*(methyl 3-*O*-benzoyl-4,5:7,8-di-*O*-isopropylidene-α-*D*-glycero-*D*-talo-2-octulopyranosonate)-(2→6)-2-azido-3,4-di-*O*-benzyl-2-deoxy-β-*D*-glucopyranoside **23***

A solution of **22** (100 mg, 190 μmol) and donor **15** (152 mg, 266 μmol) in dry CH_2Cl_2 (3 mL) was cooled to −20°C under argon atmosphere. Then TMSOTf (20 μL, 106 μmol) was added to the solution. After 3 h at −15°C, the reaction was allowed to reach room temperature (5 min), neutralised with NEt_3 (1 mL) and concentrated. Flash chromatography (toluene:EtOAc, 20:1) of the residue gave **23** (102 mg, 56%) and **17** (54 mg, 47%) as white foams; TLC (toluene:EtOAc, 2:1): R_f 0.75; $[\alpha]_D$ +22.1 (*c* 0.5, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 0.18, 0.20 [2s, 6H, $Si(CH_3)_2$], 0.87–0.90 [m, 12H, $SiC(CH_3)_2CH(CH_3)_2$], 1.19, 1.28, 1.41, 1.47 [4s, 12H, $C(CH_3)_2$], 1.62–1.68 [m, 1H, $SiC(CH_3)_2CH(CH_3)_2$], 3.29–3.31 (m, 2H, 2a-, 4a-H), 3.40 (dd, 1H, $J_{2a,3a}$=9.2 Hz, $J_{3a,4a}$=9.4 Hz, 3a-H), 3.49–3.53 (m, 6H, 5a-, 6a-, 6′a-, $COOCH_3$), 3.94 (dd, 1H, $J_{5b,6b}$=2.9 Hz, $J_{6b,7b}$=6.7 Hz, 6b-H), 4.13 (dd, 1H, $J_{8b,8'b}$=8.8 Hz, $J_{7b,8b}$=5.2 Hz, 8b-H), 4.17 (dd, 1H, $J_{7b,8'b}$=6.2 Hz, 8′b-H), 4.27 (dd, 1H, $J_{4b,5b}$=6.0 Hz, 5b-H), 4.45–4.51 (m, 3H, 1a-, 7b-H, CH_2Ph), 4.58 (dd, 1H, $J_{3b,4b}$=5.3 Hz, 4b-H), 4.76–4.91 (m, 3H, CH_2Ph), 5.46 (d, 1H, 3b-H), 7.20–8.02 (m, 15H, Ph); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ: −3.4, −2.0 [2C, $Si(CH_3)_2$], 18.4–33.9 [10C, $SiC(CH_3)_2CH(CH_3)_2$, $C(CH_3)_2$], 52.5 (1C, $COOCH_3$), 64.0 (1C, 6a-C), 66.4 (1C, 8b-C), 67.7 (1C, 3b-C), 68.6 (1C, 2a-C), 69.2 (1C, 6b-C), 70.0 (1C, 5b-C), 70.1 (1C, 4b-C), 74.0 (1C, 5a-C), 74.1 (1C, 7b-C), 74.9, 75.4 (2C, CH_2Ph), 78.0 (1C, 4a-C), 83.0 (1C, 3a-C), 96.7 (1C, 1a-C), 99.5 (1C, 2b-C), 109.3, 110.0 [2C, $C(CH_3)_2$], 127.9–137.9 (18C, Ph), 165.0, 166.3 (2C, 1b-C, COPh). Anal. calcd for $C_{50}H_{67}N_3O_{14}Si$ (962.18): C, 62.42; H, 7.02; N, 4.37; found: C, 62.43; H, 6.92; N, 4.02.

3.22. Thexyldimethylsilyl O-*(methyl 4,5:7,8-di-*O*-isopropylidene-α-*D*-glycero-*D*-talo-2-octulo-pyranosonate)-(2→6)-2-azido-3,4-di-*O*-benzyl-2-deoxy-β-*D*-glucopyranoside **24***

A solution of **23** (460 mg, 0.48 mmol) in dry MeOH (10 mL) was treated with 1 M MeONa in MeOH (0.5 mL) and stirred for 24 h at 30°C. The reaction mixture was neutralised with satd. aqueous NH_4Cl and extracted with EtOAc. Then the organic layer was dried ($MgSO_4$), concentrated in vacuo and the

residue was purified by flash chromatography (toluene:EtOAc, 4:1) to afford **24** (371 mg, 91%); TLC (toluene:EtOAc, 2:1): R_f 0.43; $[\alpha]_D$ +13.4 (*c* 0.5, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ: 0.16, 0.19 [2s, 6H, $Si(CH_3)_2$], 0.87–0.90 [m, 12H, $SiC(CH_3)_2CH(CH_3)_2$], 1.36, 1.40, 1.50 [3s, 12H, $C(CH_3)_2$], 1.55–1.70 [m, 1H, $SiC(CH_3)_2CH(CH_3)_2$], 2.79 (d, 1H, $J_{3b,OH}$=8.1 Hz, OH), 3.23–3.52 (m, 6H, 2a-, 3a-, 4a-, 5a-, 6a-, 6′a-H), 3.40 (s, 3H, $COOCH_3$), 3.74 (dd, 1H, $J_{5b,6b}$=2.7 Hz, $J_{6b,7b}$=7.8 Hz, 6b-H), 3.89 (dd, 1H, $J_{3b,4b}$=4.2 Hz, 3b-H), 3.98 (dd, 1H, $J_{8b,8'b}$=8.9 Hz, $J_{7b,8b}$=4.9 Hz, 8b-H), 4.11 (dd, 1H, $J_{7b,8'b}$=7.4 Hz, 8′b-H), 4.25 (dd, 1H, $J_{4b,5b}$=6.4 Hz, 5b-H), 4.37–4.91 (m, 7H, 4b-, 7b-, 1a-H, CH_2Ph), 7.14–7.35 (m, 10H, Ph). Anal. calcd for $C_{43}H_{63}N_3O_{13}Si$ (858.07): C, 60.19; H, 7.40; N, 4.90; found: C, 62.20; H, 7.40; N, 4.64.

3.23. Thexyldimethylsilyl O-*(methyl 4,5:7,8-di*-O-*isopropylidene-3*-O-*thiobenzoyl-α*-D-glycero-D-talo-*2-octulopyranosonate)-(2→6)-2-azido-3,4-di*-O-*benzyl-2-deoxy-β*-D-*glucopyranoside* ***25***

N,*N*-Dimethyl-α-chlorobenzimidium chloride (138 mg, 0.68 mmol) was added to a solution of **24** (290 mg, 0.34 mmol) in dry CH_2Cl_2:pyridine (10:1, 10 mL). After 24 h at room temperature, the mixture was treated with H_2S for 5 min. Then satd. aqueous $NaHCO_3$ was added and the mixture was extracted with EtOAc. The organic layer was dried ($MgSO_4$), concentrated in vacuo and the residue was purified by flash chromatography (toluene:EtOAc, 15:1) to give **25** (310 mg, 94%) as a yellow syrup; TLC (toluene:EtOAc, 2:1): R_f 0.80; $[\alpha]_D$ −17.3 (*c* 0.5, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ: 0.11 [s, 6H, $Si(CH_3)_2$], 0.86–0.90 [m, 12H, $SiC(CH_3)_2CH(CH_3)_2$], 1.15, 1.25, 1.37, 1.45 [4s, 12H, $C(CH_3)_2$], 1.62–1.74 [m, 1H, $SiC(CH_3)_2CH(CH_3)_2$], 3.23–3.51 (m, 9H, 2a-, 3a-, 4a-, 5a-, 6a-, 6′a-H, $COOCH_3$), 3.96 (dd, 1H, $J_{5b,6b}$=3.0 Hz, $J_{6b,7b}$=6.8 Hz, 6b-H), 4.12 (dd, 1H, $J_{8b,8'b}$=8.8 Hz, $J_{7b,8b}$=5.2 Hz, 8b-H), 4.17 (dd, 1H, $J_{7b,8'b}$=6.2 Hz, 8′b-H), 4.30 (dd, 1H, $J_{4b,5b}$=6.3 Hz, 5b-H), 4.41–4.53 (m, 3H, 1a-, 7b-H, CH_2Ph), 4.69 (dd, 1H, $J_{3b,4b}$=5.3 Hz, 4b-H), 4.72–4.92 (m, 3H, CH_2Ph), 6.29 (d, 1H, 3b-H), 7.16–8.16 (m, 15H, Ph); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ: −3.4, −1.9 [2C, $Si(CH_3)_2$], 18.4–33.9 [10C, $SiC(CH_3)_2CH(CH_3)_2$, $C(CH_3)_2$], 52.4 (1C, $COOCH_3$), 64.0 (1C, 6a-C), 66.6 (1C, 8b-C), 68.7 (1C, 2a-C), 69.7 (1C, 6b-C), 70.4 (1C, 4b-C), 70.5 (1C, 5b-C), 73.9 (1C, 3a-C), 74.2 (1C, 7b-C), 74.8, 75.4 (2C, CH_2Ph), 78.0 (1C, 5a-C), 83.2 (1C, 4a-C), 96.8 (1C, 1a-C), 99.3 (1C, 2b-C), 109.3, 110.2 [2C, $C(CH_3)_2$], 127.9–138.1 (18C, Ph), 166.2, (1C, 1b-C), 210.2 (1C, CSPh); MALDI-MS: $[M+Na]^+$=1001, $[M+K]^+$=1017. Anal. calcd for $C_{50}H_{67}N_3O_{13}SSi$ (978.24): C, 61.39; H, 6.90; N, 4.30; found: C, 61.04; H, 6.75; N, 4.10.

3.24. Thexyldimethylsilyl O-*(methyl 3-deoxy-4,5:7,8-di*-O-*isopropylidene-α*-D-manno-*2-octulo-pyranosonate)-(2→6)-2-acetamido-3,4-di*-O-*benzyl-2-deoxy-β*-D-*glucopyranoside* ***26***

A solution of **25** (110 mg, 110 μmol) in dry and degassed toluene (4 mL) was treated with Bu_3SnH (54 μL, 200 μmol) and AIBN (1.0 mg) under argon atmosphere. The mixture was heated at 90°C for 2 h, then stirred for 2 h at room temperature and evaporated to dryness. The residue was dissolved in pyridine:water (3:1, 5 mL) and treated with H_2S for 5 min. After 36 h at room temperature, the mixture was evaporated to dryness, dissolved in pyridine:Ac_2O (2:1, 8 mL) and stirred overnight. Concentration in vacuo and flash chromatography of the residue (toluene:EtOAc, 3:1) afforded **26** (68 mg, 70%) as a colourless syrup; TLC (toluene:EtOAc, 1:1): R_f 0.53; $[\alpha]_D$ +10.5 (*c* 0.5, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ: 0.10–0.13 [2s, 6H, $Si(CH_3)_2$], 0.80–0.84 [m, 12H, $SiC(CH_3)_2CH(CH_3)_2$], 1.29, 1.35, 1.37, 1.38 [4s, 12H, $C(CH_3)_2$], 1.52–1.59 [m, 1H, $SiC(CH_3)_2CH(CH_3)_2$], 1.80–1.87 (m, 4H, 3b-H, $NHCOCH_3$), 2.74 (dd, 1H, $J_{3'b,4b}$=4.2 Hz, $J_{3b,3'b}$=15.3 Hz, 3′b-H), 3.32–3.69 (m, 9H, 3a-, 4a-, 5a-, 6a-, 6′a-, 6b-H, $COOCH_3$), 3.93–4.02 (m, 2H, 8b-, 2a-H), 4.10 (dd, 1H, $J_{7b,8'b}$=6.2 Hz, 8′b-H), 4.24 (dd, 1H, $J_{4b,5b}$=7.6 Hz, $J_{5b,6b}$=1.7

Hz, 5b-H), 4.35 (ddd, 1H, $J_{6b,7b}$=7.8 Hz, $J_{7b,8b}$=4.8 Hz, 7b-H), 4.46–4.80 (m, 5H, 4b-H, CH_2Ph), 4.92 (d, 1H, $J_{1a,2a}$=7.5 Hz, 1a-H), 5.37 (d, 1H, $J_{2a,NH}$=8.2 Hz, NH), 7.11–7.32 (m, 10H, Ph); MALDI-MS: $[M+Na]^+$=881, $[M+K]^+$=897. Anal. calcd for $C_{45}H_{67}NO_{13}Si$ (858.11): C, 62.99; H, 7.87; N, 1.63; found: C, 62.80; H, 7.72; N, 1.38.

3.25. *Acetyl* O-*(methyl 4,5,7,8-tetra*-O-*acetyl-3-deoxy-α*-D-manno-*2-octulopyranosonate)-(2→6)-2-acetamido-3,4-di*-O-*benzyl-2-deoxy-α,β*-D-*glucopyranoside* ***27***

Aqueous 80% trifluoroacetic acid (1 mL) was added to a solution of **26** (50 mg, 58 μmol) in CH_2Cl_2 (5 mL). The mixture was stirred for 24 h at room temperature, then concentrated and coevaporated several times with toluene. The residue was dissolved in pyridine:Ac_2O (2:1, 7 mL) and stirred for 24 h at room temperature. Then the reaction mixture was concentrated in vacuo and the residue was purified by flash chromatography (toluene:EtOAc, 1:2) to give **27** (28 mg, 55%); TLC (EtOAc): R_f 0.47; **α**: ^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.78–2.11 (m, 19H, $COCH_3$, 3b-H), 2.15 (dd, 1H, $J_{3b,3'b}$=12.9 Hz, $J_{3'b,4b}$=5.6 Hz, 3′b-H), 3.49–3.53 (m, 2H, 6a-, 4a-H), 3.67–3.74 (m, 5H, 3a-, 6′a-H, $COOCH_3$), 3.79 (ddd, 1H, $J_{5a,6a}$=6.5 Hz, $J_{5a,6'a}$=2 Hz, $J_{4a,5a}$=10.5 Hz, 5a-H), 4.02 (dd, 1H, $J_{7b,8b}$=5.3 Hz, $J_{8b,8'b}$=12.2 Hz, 8b-H), 4.12 (dd, 1H, $J_{5b,6b}$=1 Hz, $J_{6b,7b}$=9.7 Hz, 6b-H), 4.27 (ddd, 1H, $J_{1a,2a}$=3.8 Hz, $J_{2a,3a}$=10.6 Hz, $J_{2a,NH}$=9.1 Hz, 2a-H), 4.54 (dd, 1H, $J_{7b,8'b}$=2.6 Hz, 8′b-H), 4.85–4.92 (m, 5H, CH_2Ph, NH), 5.20–5.18 (ddd, 1H, 7b-H), 5.21 (ddd, 1H, $J_{4b,5b}$=2 Hz, $J_{3b,4b}$=12.0 Hz, 4b-H), 5.29 (bs, 1H, 5b-H), 6.01 (d, 1H, 1a-H), 7.28–7.36 (m, 10H, Ph); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ: 20.7–23.2 (6C, CO*C*H_3), 31.9 (1C, 3b-C), 51.4 (1C, 2a-C), 52.8 (1C, COO*C*H_3), 62.4 (1C, 8b-C), 62.9 (1C, 6a-C), 64.6 (1C, 5b-C), 66.2 (1C, 4b-C), 67.6 (1C, 7b-C), 68.4 (1C, 6b-C), 72.5 (1C, 5a-C), 74.8, 75.2 (2C, *C*H_2Ph), 78.4 (1C, 4a-C), 79.6 (1C, 3a-C), 91.0 (1C, 1a-C), 98.5 (1C, 2b-C), 127.9–137.7 (12C, Ph), 168.8–170.5 (7C, 1b-C, *C*OCH_3); **β**: ^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.76–2.16 (7s, 20H, $COCH_3$, 3b-, 3′b-H), 3.50–5.29 (m, 13H, 2a-, 3a-, 4a-, 5a-, 6a-, 6′a-, 4b-, 5b-, 6b-, 7b-, 8b-, 8′b-H, NH), 5.65 (d, 1H, $J_{1a,2a}$=7.5 Hz, 1a-H), 7.28–7.37 (m, 10H, Ph); FAB-MS (nominal mass): $[M+Na]^+$=868, $[M+NaI]Na^+$=1018; MALDI-MS: $[M+Na]^+$=869, $[M+K]^+$=885. Anal. calcd for $C_{41}H_{51}NO_{18}\cdot 2H_2O$ (881.88): C, 55.84; H, 6.28; N, 1.59; found: C, 55.89; H, 6.18; N, 1.34.

3.26. *Thexyldimethylsilyl* O-*(methyl 3*-O-*acetyl-4,5:7,8-di*-O-*isopropylidene-α*-D-glycero-D-talo-*2-octulopyranosonate)-(2→6)-2-acetamido-3,4-di*-O-*benzyl-2-deoxy-β*-D-*glucopyranoside* ***28***

A solution of **24** (150 mg, 0.175 mmol) in pyridine:water (3:1, 5 mL) was treated with H_2S and stirred for 36 h. The mixture was evaporated to dryness and acetylated with pyridine:Ac_2O (2:1, 6 mL) and DMAP (10 mg) for 12 h. After concentration in vacuo, the residue was purified by flash chromatography (toluene:EtOAc, 4:1) to afford **28** (125 mg, 78%); TLC (toluene:EtOAc, 2:1): R_f 0.33; $[\alpha]_D$ +21.0 (*c* 0.5, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ: 0.09–0.10 [2s, 6H, $Si(CH_3)_2$], 0.79–0.84 [m, 12H, $SiC(CH_3)_2CH(CH_3)_2$], 1.32, 1.38, 1.42, 1.46 [4s, 12H, $C(CH_3)_2$], 1.54–1.60 [m, 1H, $SiC(CH_3)_2CH(CH_3)_2$], 1.82 (s, 3H, $NHCOCH_3$), 2.06 (s, 3H, $COCH_3$), 3.28–3.33 (m, 2H, 2a-, 4a-H), 3.46 (dd, 1H, $J_{5a,6a}$=8.2 Hz, $J_{6a,6'a}$=10.1 Hz, 6a-H), 3.52 (dd, 1H, $J_{5a,6'a}$=2.7 Hz, 6′a-H), 3.61 (ddd, 1H, $J_{4a,5a}$=8.6 Hz, 5a-H), 3.63 (s, 3H, $COOCH_3$), 3.81 (dd, 1H, $J_{4b,5b}$=7.4 Hz, $J_{5b,6b}$=3.0 Hz, 5b-H), 4.03 (dd, 1H, $J_{7b,8b}$=4.9 Hz, $J_{8b,8'b}$=8.9 Hz, 8b-H), 4.08 (dd, 1H, $J_{2a,3a}$=8.4 Hz, $J_{3a,4a}$=9.9 Hz, 3a-H), 4.11 (dd, 1H, $J_{7b,8'b}$=6.2 Hz, 8′b-H), 4.24 (dd, 1H, $J_{6b,7b}$=6.7 Hz, 6b-H), 4.44–4.80 (m, 6H, 4b-, 7b-H, CH_2Ph), 4.95 (d, 1H, $J_{1a,2a}$=7.7 Hz, 1a-H), 5.25 (d, 1H, $J_{3b,4b}$=5.2 Hz, 3b-H), 5.43 (d, 1H, $J_{2a,NH}$=8.2 Hz, NH), 7.16–7.34 (m, 10H, Ph); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ: −3.7, −1.8 [2C, $Si(CH_3)_2$], 18.5–34.0 [12C, $SiC(CH_3)_2CH(CH_3)_2$, $COCH_3$, $C(CH_3)_2$], 52.2 (1C, $COOCH_3$), 58.6 (1C, 2a-C), 64.2 (1C, 6a-C), 66.6

(1C, 8b-C), 67.4 (1C, 3b-C), 69.4 (1C, 5b-C), 70.2 (2C, 4b-, 6b-C), 73.5 (1C, 5a-C), 73.9 (1C, 7b-C), 74.4 (2C, *C*H_2Ph), 78.9 (1C, 4a-C), 80.3 (1C, 3a-C), 94.6 (1C, 1a-C), 99.4 (1C, 2b-C), 109.4, 109.9 [2C, *C*$(CH_3)_2$], 127.9–138.4 (12C, Ph), 166.3, 169.3, 170.0 (3C, 1b-C, *C*OCH_3); MALDI-MS: $[M+Na]^+$=939. Anal. calcd for $C_{47}H_{69}NO_{15}Si\cdot 2H_2O$ (952.18): C, 59.29; H, 7.73; N, 1.47; found: C, 59.27; H, 7.69; N, 1.27.

3.27. Acetyl O-*(methyl 3,4,5,7,8-penta*-O-*acetyl-α*-D-glycero-D-talo-*2-octulopyranosonate)-(2→6)-2-acetamido-3,4-di*-O-*benzyl-2-deoxy-α,β*-D-*glucopyranoside* ***29***

Aqueous 80% trifluoroacetic acid (2 mL) was added to a solution of **28** (105 mg, 110 μmol) in CH_2Cl_2 (10 mL). The mixture was stirred for 24 h at room temperature, then concentrated and co-evaporated several times with toluene. The residue was dissolved in 10 mL of pyridine:Ac_2O (2:1) and stirred for 24 h at room temperature. Then the reaction mixture was concentrated in vacuo and the residue was purified by flash chromatography (toluene:EtOAc, 1:2) to give **29** (55 mg, 55%); TLC (EtOAc): R_f 0.46; **α**: ^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.77–2.11 (5s, 21H, $COCH_3$), 3.47 (dd, 1H, $J_{4a,5a}$=8.5 Hz, $J_{3a,4a}$=10.3 Hz, 4a-H), 3.48 (dd, 1H, $J_{6a,6'a}$=10.3 Hz, $J_{5a,6a}$=7.0 Hz, 6a-H), 3.53 (dd, 1H, $J_{5a,6'a}$=2 Hz, 6′a-H), 3.62–3.92 (m, 4H, 3a-H, $COOCH_3$), 3.80 (ddd, 1H, 5a-H), 4.08 (dd, 1H, $J_{7b,8b}$=5.0 Hz, $J_{8b,8'b}$=12.0 Hz, 8b-H), 4.22–4.26 (m, 2H, 2a-, 6b-H), 4.54–4.94 (m, 5H, 8′b-H, CH_2Ph), 5.22 (dd, 1H, $J_{3b,4b}$=3.8 Hz, $J_{4b,5b}$=3.5 Hz, 4b-H), 5.27 (dd, 1H, $J_{5b,6b}$=1 Hz, 5b-H), 5.29–5.33 (m, 2H, 7b-H, NH), 5.42 (d, 1H, 3b-H), 5.98 (d, 1H, $J_{1a,2a}$=3.8 Hz, 1a-H), 7.18–7.38 (m, 10H, Ph); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ: 20.4–23.2 (7C, CO*C*H_3), 51.3 (1C, 2a-C), 52.7 (1C, COO*C*H_3), 62.2 (1C, 8b-C), 63.0 (1C, 6a-C), 63.9 (1C, 5b-C), 65.7 (1C, 4b-C), 67.4 (2C, 3b-, 7b-C), 68.4 (1C, 6b-C), 72.1 (1C, 5a-C), 74.9, 75.2 (2C, *C*H_2Ph), 78.3 (1C, 4a-C), 79.6 (1C, 3a-C), 90.8 (1C, 1a-C), 98.9 (1C, 2b-C), 127.9–137.8 (12C, Ph), 165.3–170.5 (8C, 1b-C, *C*OCH_3); **β**: ^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.79–2.11 (7s, 21H, $COCH_3$), 3.44–5.38 (m, 13H, 2a-, 3a-, 4a-, 5a-, 6a-, 6′a-, 4b-, 5b-, 6b-, 7b-, 8b-, 8′b-H, NH), 5.45 (d, 1H, $J_{3b,4b}$=1 Hz, 3b-H), 5.64 (d, 1H, $J_{1a,2a}$=7.3 Hz, 1a-H), 7.18–7.38 (m, 10H, Ph); MALDI-MS: $[M+Na]^+$=926, $[M+K]^+$=942. Anal. calcd for $C_{43}H_{53}NO_{20}\cdot\frac{1}{2}H_2O$ (912.90): C, 56.02; H, 6.02; N, 1.52; found: C, 56.02; H, 5.88; N, 1.42.

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