DOI: 10.1002/ejoc.200600851

# Glycosylation under Thermodynamic Control: Synthesis of the Di- and the Hexasaccharide Fragments of the O-SP of *Vibrio Cholerae* O:1 Serotype Ogawa from Fully Functionalized Building Blocks

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**Keywords:** Carbohydrates / Oligosaccharides / Synthetic methods / Thioglycosides / Cholera vaccine

The known 5-(methoxycarbonyl)pentyl α-glycoside of the hexasaccharide of the O-SP of *Vibrio cholerae* O:1, serotype Ogawa **31** was newly prepared from side-chain-equipped disaccharide building blocks. The intermediate tetrasaccharide **25** was prepared from the disaccharide glycosyl acceptor **11** and the (1→2)-linked disaccharide thioglycoside glycosyl donor **8**, having a (non-participating) saccharide moiety at C-2 in the downstream end. When performed conventionally (at room or at sub 0 °C temperatures), glycosylations with **11**, carried out without anchimeric assistance, showed poor stereoselectivity but the formation of the 1,2-*trans*-glycosidic linkage could be markedly improved through thermodynamic control. This synthetic strategy towards **31** was more efficient than the step-wise approach, which was based on iterative glycosylation of **11** with **5** followed by delevulinoylation. Thermodynamic control improved considerably the yields of glycosylation of tetrasaccharide glycosyl acceptor **26** with disaccharide donor **18**, to give the fully protected hexasaccharide **28**, and also a similar reaction of the thioglycoside **18** with methyl 5-hydroxyhexanoate, to afford the linker-equipped disaccharide **19**. Sequential deacetylation and debenzylation of the hexasaccharide **28**, and deprotection of one of its intermediates, **19**, gave the target hexasaccharide **31**, and the wanted disaccharide **22**, respectively.



## Introduction

Cholera is a very serious enteric disease caused by the bacterium *Vibrio cholerae*. Intestinal infection is usually followed by severe diarrhea with dehydration, rapid loss of bodily fluids and electrolytes, which can quickly lead to death. More than 200 serogroups of *V. cholerae* have been identified[1] differing in the structure of their O-specific polysaccharide (O-PS). Until 1992, when a new serogroup O:139 caused a cholera epidemic in the Indian subcontinent, the O:1 strain was thought to be the only *Vibrio cholerae* bacterium pathogenic in humans.[2] *Vibrio cholerae* O:1 occurs as two serotypes, Ogawa and Inaba, whose O-PS are linear homopolymers of α-(1→2)-linked 3-deoxy-L-*glycero*-tetronamido-D-perosamine.[3] The upstream perosamine unit is 2-*O*-methylated only in the Ogawa serotype.[4–6]

Oligosaccharides composed of *N*-acylated amino sugars can be built up by two strategies. The most common one[7–9] consists in constructing the oligosaccharide from azido sugars, which are eventually transformed into their *N*-acylamido counterparts. In the alternative approach,[10,11] the oligosaccharide is constructed from intermediates having the acylamido side chain already in place, thus minimizing the number of chemical manipulations with the higher oligosaccharides. The latter synthetic strategy requires a set of selectively removable protecting groups in intermediates. To improve on our previous strategy[11] we have recently reported[12] preparation of the 1-thio-α-perosaminide **5**. It has the 4-amino group functionalized with 2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronic acid,[13] and is a potentially useful synthon in the preparation of higher oligosaccharides in the *Vibrio cholerae* O:1 series. The stable benzyl group at position 3 in **5** eliminates problems of acyl group migration we experienced[11] during glycosylations when the acetyl group was at that position. The levulinoyl group at position 2 can be selectively removed in the presence of acetyl groups in the N-side-chain, and is capable of anchimeric assistance in the glycosylation reactions.[12,14,15]

Utility of neoglycoconjugates from 5-(methoxycarbonyl)-pentyl α-glycosides of di- and hexasaccharide fragments (**22** and **31**, respectively) of the O-SP of *Vibrio cholerae* O:1, serotype Ogawa, as experimental vaccines has already been proven.[16,17] Within our efforts to develop a clinically useful vaccine for cholera, we explore, among other things, possibilities to improve existing synthetic strategies towards the foregoing oligosaccharides. Here we describe a new synthetic approach towards antigens **22** and **31** from fully functionalized building blocks. We also compare the block-wise and the step-wise assembly of the key tetrasaccharide intermediate **25**, using the side chain-equipped monosaccharide **5** and disaccharide **8** as glycosyl donors.

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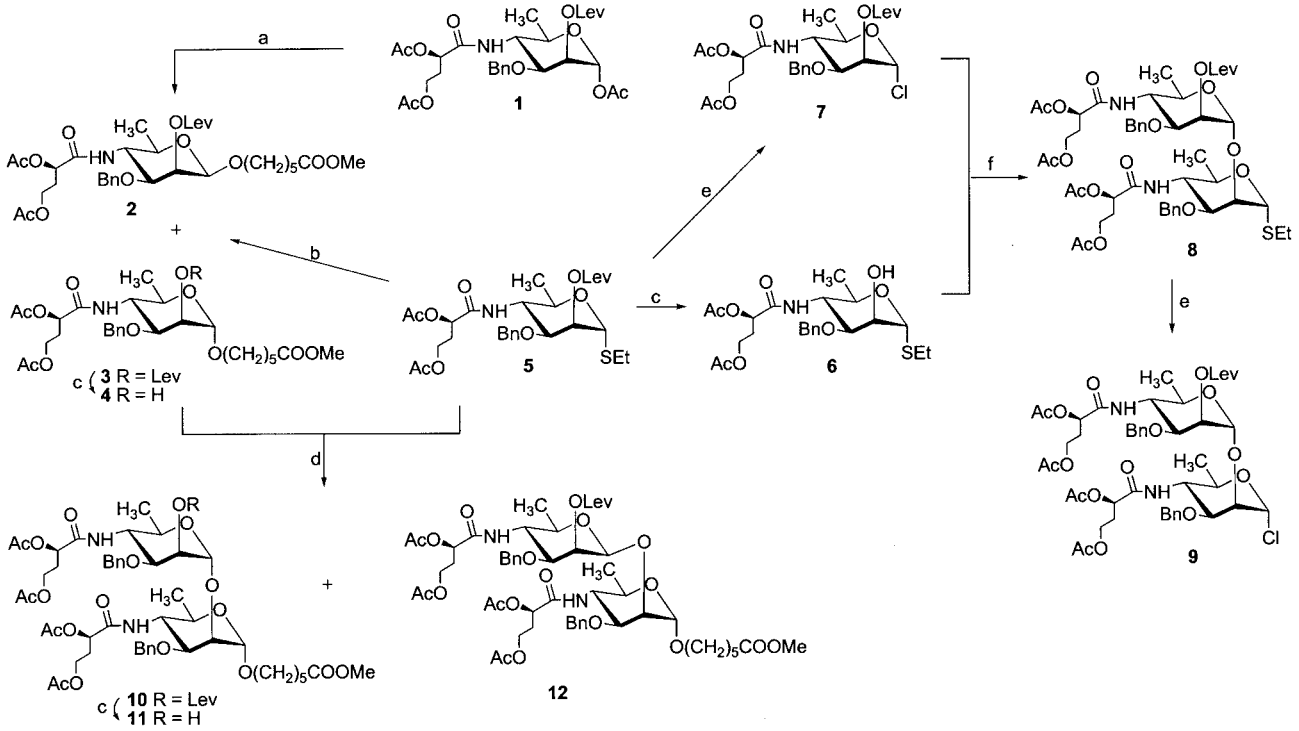
## Results and Discussion

Our previous syntheses[11,18–22] of higher oligosaccharides in the *Vibrio cholerae* O:1 series had their shortcomings due to either instability of protecting groups, lack of stereoselectivity of glycosylation reactions, or separation problems involved. Also, losses resulting from multiple chemical manipulations with high oligosaccharides we experienced during some previous approaches suggested that, rather than a stepwise approach, a suitable block wise strategy using fully functionalized intermediates as building blocks should be pursued. Therefore, in the present synthesis of the Ogawa hexasaccharide **31** from side-chain-equipped building blocks, we first prepared the disaccharide glycosyl acceptor **11** by NIS/AgOTf-promoted glycosylation of **4** with the known[12] thioglycoside **5** to give **10**, followed by selective removal of the Lev ester group (Scheme 1).

The linker-equipped α-glycoside **3** was prepared in 88% yield from the known acetate **1**[12] and methyl 6-hydroxyhexanoate by $BF_3{\cdot}Et_2O$-promoted glycosylation. Alternatively, glycosylation of methyl 6-hydroxyhexanoate with **5** was mediated with NIS/AgOTf. The latter reaction was less stereoselective giving **3** in 70% yield, together with the β anomer **2** (20%). After cleavage of the Lev group, the obtained 2-hydroxy sugar **4** was coupled with **5**, to form the desired 1,2-*trans*-linked disaccharide with high stereoselectivity: the α (**10**) and β product (**12**) were obtained in 80 and 6% yield, respectively.

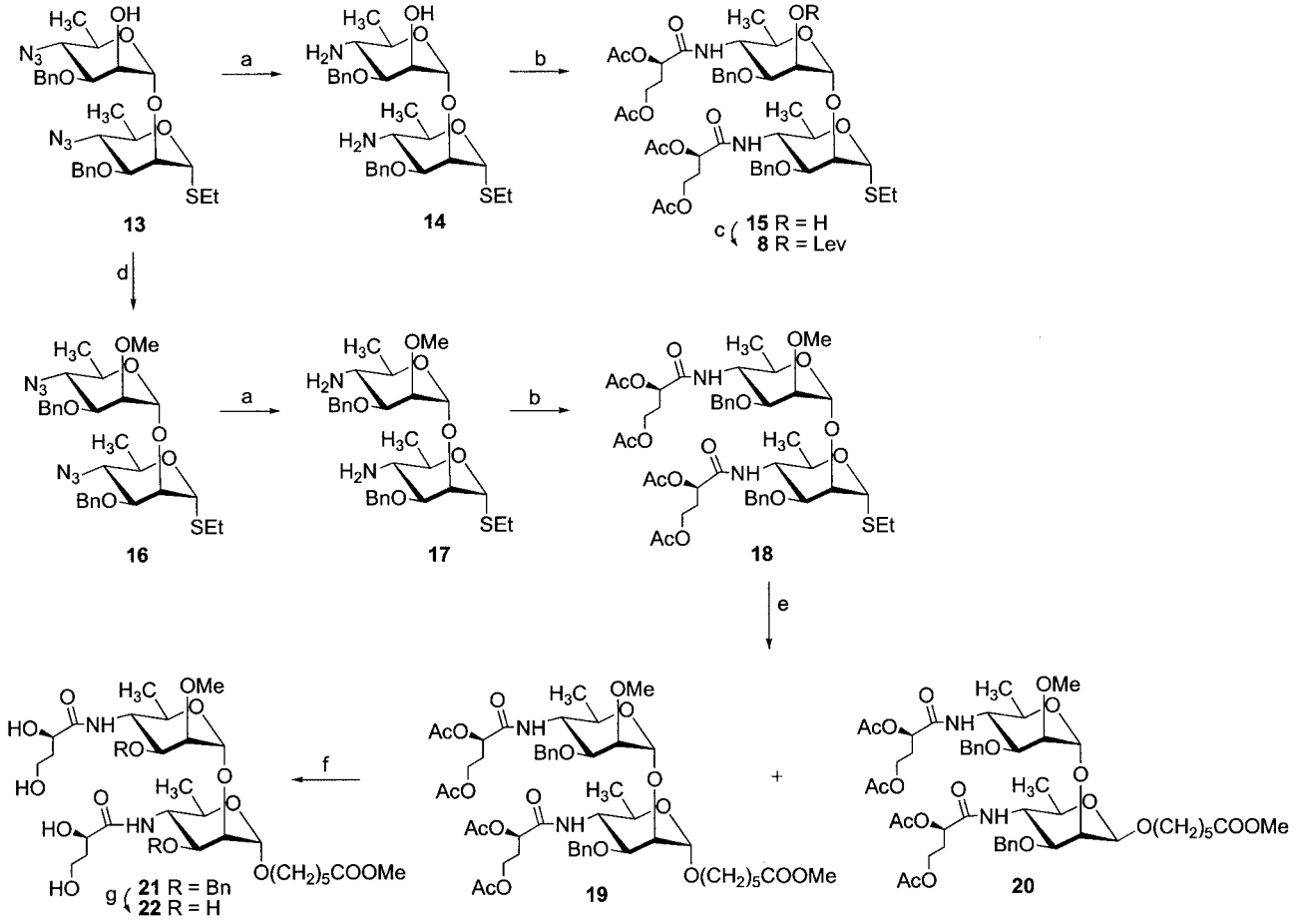
The disaccharide donor **8** was obtained by coupling of the thioglycoside **6**, prepared from **5** by cleavage of the Lev group, with the crystalline chloride **7**, given rise to readily by treatment[23] of **5** with $Cl_2$ in $CCl_4$ (Scheme 1). The reaction mixture contained mainly **8** but a number of by-products were also formed. The yield of **8** was much lower (58%) than what would be expected from the outcome of a similar conversions leading to the 2-*O*-acetyl derivative of the diazido disaccharide **13** lacking the amido group.[19,24] The thioglycoside **5** was one of the by-products (isolated in 10% yield), showing that the low yield of **8** was, at least partially, due to the transfer of the strongly nucleophilic ethanethio group from the thioglycoside acceptor **6** to the chloride donor **7**. Similar transformations have been observed.[25–27]

Having alcohol **11** at hand, it appeared that methylation at O-2 followed by deprotection would readily give one of the target products, the disaccharide **22**. However, all attempts to methylate the disaccharide **11** failed due to acetyl protecting groups which were labile in both basic or acidic conditions. Unsuccessful conversions **11**→**19** (MeI/AgO, MeOTf/$Et_3SiOTf$, or $CH_2N_2/BF_3{\cdot}Et_2O$; these reactions are not described in the Exp. Sect.) and low yield of the conversion **6** + **7**→**8** prompted us to prepare the disaccharide donors **8** and **18** from the known diazido disaccharide **13**[19,24] (Scheme 2). Accordingly, after selective reduction[28] of **13** (→**14**), followed by amidation with 2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronic acid[13] (**14**→**15**), esterification of **15** with levulinic acid in the presence of EDAC/4-Dimethylaminopyridine provided the disaccharide thioglycoside **8** (82%) in three steps. A similar synthetic scheme was applied to prepare the 2-*O*-methylated disaccharide **18**. Methylation[29,30] of **13** (→**16**), followed by reduction[28] of




Scheme 1. a: $HO(CH_2)_5COOMe$, $BF_3{\cdot}Et_2O$, $CH_2Cl_2$; b: $HO(CH_2)_5COOMe$, NIS, AgOTf, $CH_2Cl_2$; c: $H_2NNH_2{\cdot}AcOH/CH_2Cl_2$, MeOH; d: NIS, AgOTf, $CH_2Cl_2$; e: $Cl_2$, $CCl_4$; f: AgOTf, TMU, $CH_2Cl_2$.




Scheme 2. a: $H_2S$, Py/$H_2O$, 40 °C; b: 2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronic acid, EDAC, $CH_2Cl_2$; c: LevOH, EDAC, 4-(dimethylamino)pyridine, $CH_2Cl_2$; d: MeI, KOH, $Me_2SO$; e: $HO(CH_2)_5COOMe$, NIS, AgOTf, $CH_2Cl_2$; f: NaOMe, MeOH; g: $H_2$, Pd/C, MeOH.

the azido groups with $H_2S$ afforded the diamino disaccharide **17**, which was readily converted into the desired, crystalline disaccharide donor **18**.

Glycosidation of **18** with 5-(methoxycarbonyl)pentanol was carried out at various conditions to optimize the yield of the linker-equipped disaccharide **19**. Effect of various reaction conditions are shown in Table 1. While the reaction at room temperature and $CH_2Cl_2$ as solvent produced a mixture of anomers (α:β = 1:1, Entry 1), the amount of the β anomer **20** slightly increased using $CH_3CN$ as solvent (Entry 3) or when the reaction was conducted at –20 °C using $CH_2Cl_2$ as solvent (Entry 5). Addition of ether type solvents to the reaction mixture, e.g. toluene/dioxane (1:4), has been reported to have α-directional effect on glycosylation[31] but applying those conditions (Table, Entry 2) did not change the situation. Better α selectivity in the synthesis of **19** was achieved by thermodynamic control of the reaction, namely by conducting the reaction at higher temperature (see Exp. Sect. and Table 1, Entry 6 and 7). The amount of the thermodynamically more stable α anomer almost doubled when the reaction was performed at reflux temperature (see Exp. Sect. and Table 1) and the compounds **19** and **20** were formed in a ratio of 1.8:1. Two-step deprotection of the α-glycoside **19** gave the target disaccharide **22**, which was identical with the independently synthesized substance.[32] Using a higher-field instrument than during the original work,[32] resonances in the NMR spectra of the substance could now be fully assigned.

To evaluate efficiency of construction of oligosaccharides in this series by various approaches we have compared results of the stepwise and blockwise synthetic strategy towards tetrasaccharide **25**. In the stepwise approach, the synthesis involved (Scheme 3) NIS/AgOTf-mediated coupling of the disaccharide acceptor **11** with donor with **5** (→**23**, 76%), followed by delevulinoylation (→**24**, ca. 100%). Subsequent glycosylation of **24** with **5** gave **25** (81%).

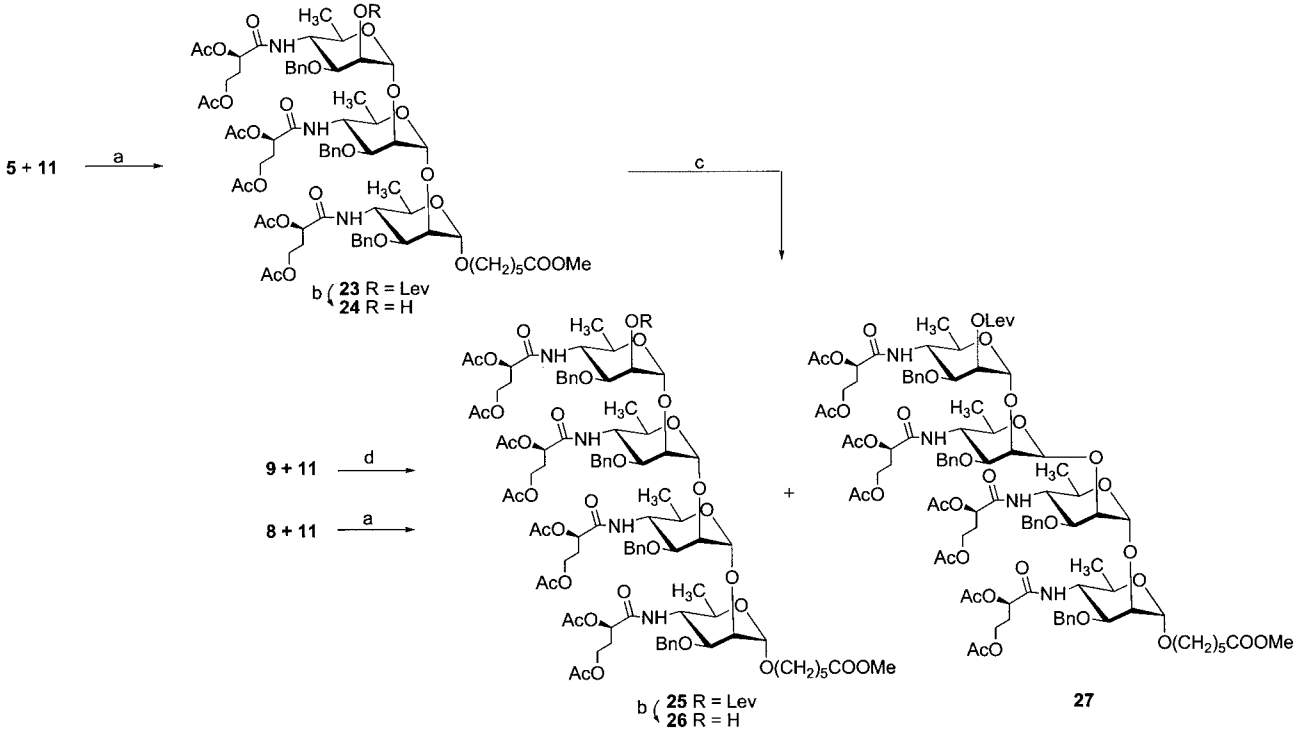
In the blockwise, NIS/AgOTf-mediated construction of the tetrasaccharide **25** from the disaccharide donor **8** and the acceptor **11**, the reaction conducted at room temperature gave a mixture of α- and β-linked tetrasaccharides **25** and **27**, respectively, in a ratio of 2:1 (Table 1, Entry 8; combined yield 80%). Very similar, closely related 4-azido-oligosaccharides made by blockwise assembly from intermediates lacking the acylamido group, were obtained with much better α stereoselectivity.[22,24,33] Attempts to improve the yield of **25** by changing the glycosyl donor and promoter were unsuccessful (Table 1, Entry 9). The latter two obser-

Table 1. Effect of solvent and temperature on stereoselectivity of glycosylation.[a]

| Entry | Acceptor | Donor | Solvent | Procedure | Temperature[b] [°C] | Products | α:β |
|---|---|---|---|---|---|---|---|
| 1 | $MeOCO(CH_2)_5OH$ | **18** | DCM | A | room temp. | **19**, **20** | 1:1 |
| 2 | $MeOCO(CH_2)_5OH$ | **18** | 1:4 toluene/1,4-dioxane | A | room temp. | **19**, **20** | 1:1 |
| 3 | $MeOCO(CH_2)_5OH$ | **18** | MeCN | A | room temp. | **19**, **20** | 1:1.1 |
| 4 | $MeOCO(CH_2)_5OH$ | **18** | 4:1 toluene/DCM | A | room temp. | **19**, **20** | 1:1 |
| 5 | $MeOCO(CH_2)_5OH$ | **18** | DCM | A | –20 | **19**, **20** | 1:1.5 |
| 6 | $MeOCO(CH_2)_5OH$ | **18** | ca. 7:1 toluene/DCM[c] | B | 60 | **19**, **20** | 1.2:1 |
| 7 | $MeOCO(CH_2)_5OH$ | **18** | ca. 7:1 toluene/DCM[c] | B | (reflux) | **19**, **20** | 1.8:1 |
| 8 | **11** | **8** | DCM | A | room temp. | **25**, **27** | 2:1 |
| 9 | **11** | **9** | DCM | see Exp. Sect. | room temp. | **25**, **27** | 2:1 |
| 10 | **11** | **8** | ca. 7:1 toluene/DCM[c] | B | (reflux) | **25**, **27** | 5:1 |
| 11 | **26** | **18** | DCM | A | room temp. | **28**, **29** | 3:1 |
| 12 | **26** | **18** | ca. 7:1 toluene/DCM[c] | B | (reflux) | **28**, **29** | 5:1 |

[a] Determined by $^1H$ NMR spectroscopy. [b] Reaction time, 15–30 min. [c] The reaction was performed in a well-ventilated hood. Carbohydrate synthons were dissolved in a little DCM to aid solubilization, and toluene was added followed by molecular sieves. The mixture, kept in a septum-closed flask under inert gas, was then brought to reflux while DCM was allowed to escape through a needle. The rest of reagents was added when DCM largely escaped, the reagent flask was equipped with a reflux condenser, and the mixture was kept under reflux until TLC showed that the reaction was complete.

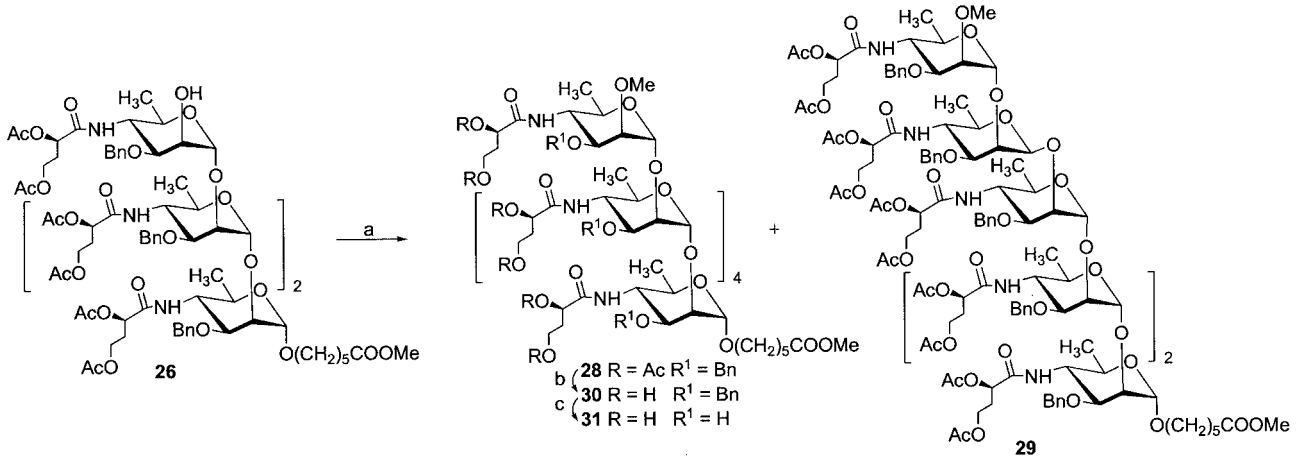



Scheme 3. a: NIS, AgOTf, $CH_2Cl_2$; b: $H_2NNH_2$·AcOH, $CH_2Cl_2$/MeOH; c: **5**, NIS, AgOTf, $CH_2Cl_2$; d: AgOTf, 2,6-di-*tert*-butyl-4-methylpyridine, $CH_2Cl_2$.

vations strongly suggest that the lower α stereoselectivity in our situation was due to the presence of the N-side chain in the building blocks involved. Nevertheless, the yield of **25** could be improved, as was the case of making the glycoside **19**, by performing the glycosylation reaction at reflux temperature: compounds **25** and **27** were formed in a combined yield of 93% (α:β = 5:1, Table 1, Entry 10). Thermodynamic control, even in absence of anchimeric assistance, and with a more hindered nucleophile than methyl 6-hydroxyhexanoate, resulted in more favored formation of the thermodynamically more stable α product. Overall, we consider the blockwise approach to compound **25** superior to the stepwise preparation. While the overall yields of the target compound are comparable, the blockwise approach requires fewer difficult purifications by chromatography (see Exp. Sect.).

To prepare the hexasaccharide **28**, the tetrasaccharide **25** was selectively deprotected at the $2^{IV}$ and compound **26** thus formed was used for glycosylation with the $2^{II}$-*O*-methylated disaccharide donor **18**. When thermodynamic control of the reaction was applied, the ratio of products formed (**28** and **29**) was increased from 3:1 (Table 1, Entry 11) to 5:1 (Table 1, Entry 12). Sequential deprotection (deacetylation, →**30**) followed by debenzylation gave the target, deprotected hexasaccharide **31**, which was identical with the previously synthesized substance.[18] More detailed




Scheme 4. a: 18, NIS, AgOTf, $CH_2Cl_2$; b: NaOMe, MeOH; c: $H_2$, Pd/C, MeOH.

assignment of NMR resonances in spectra of **31** could now be made, using the 600 MHz spectrometer (Scheme 4).

In conclusion, the known compounds **31** and **22** were newly synthesized from side-chain-equipped, fully functionalized building blocks. The poor stereoselectivity of glycosylations, compared with similar reactions involving 4-azido intermediates which lack the acylamido group at the same position,[18,22,24,33] could not be improved by the solvent effect or by changing nature of the glycosyl donor. However, glycosylations with the same reactants could be made more α-selective when they were conducted under thermodynamic control, showing that with the complex synthons involved, temperature is the key parameter to control the formation of the thermodynamically more stable α-product.

## Experimental Section

**General Methods:** Unless stated otherwise, optical rotations were measured at ambient temperature with a Perkin–Elmer automatic polarimeter, Model 341. All reactions were monitored by thin-layer chromatography (TLC) on silica gel 60 coated glass slides. Column chromatography was performed by elution from columns of silica gel with the CombiFlash Companion Chromatograph (Isco, Inc.). Solvent mixtures less polar than those used for TLC were used at the onset of separation. Nuclear Magnetic Resonance (NMR) spectra were measured at 300 MHz ($^1$H) and 75 MHz ($^{13}$C) with a Varian Gemini or Varian Mercury spectrometer, or at 600 MHz ($^1$H) and 150 MHz ($^{13}$C) with a Bruker Avance 600 spectrometer. Assignments of NMR signals were made by homonuclear and heteronuclear 2-dimensional correlation spectroscopy, run with the software supplied with the spectrometers. Assignment of $^{13}$C NMR spectra of some higher oligosaccharides was aided by comparison with spectra of related substances reported previously from this laboratory or elsewhere.[33] When the latter approach was used, to aid in the $^{13}$C NMR signal-nuclei assignments, advantage was taken of variations of line intensity expected for oligosaccharides belonging to the same homologous series.[34,35] Thus, spectra showed close similarity of chemical shifts of equivalent carbon atoms of the internal residues, and an increase in the relative intensity of these signals with the increasing number of D-perosamine residues in the molecule. When reporting assignment of NMR signals, nuclei associated with the 4-amido side chain are denoted with a prime and those with the spacer (linker) are denoted with a double prime. When reporting assignments of NMR signals, sugar residues in oligosaccharides are serially numbered, beginning with the one bearing the aglycon, and are identified by a Roman numeral superscript in listings of signal assignments. Liquid Chromatography–Electron Spray-Ionization Mass Spectrometry (ESI-MS) was performed with a Hewlett–Packard 1100 MSD spectrometer. Gas chromatography Electron Impact Mass Spectrometry (GC-EI-MS) was performed with a Hewlett–Packard 5898A spectrometer. Attempts have been made to obtain correct combustion analysis data for all new compounds. However, some compounds tenaciously retained traces of solvents, despite exhaustive drying, and analytical figures for carbon could not be obtained within ±0.4%. Structures of these compounds follow unequivocally from the mode of synthesis, NMR spectroscopic data and *m*/*z* values found in their mass spectra, and their purity was verified by TLC and NMR spectroscopy. To obtain dry silica gel, the commercial material was dried at 160 °C overnight. 5% Palladium-on-charcoal catalyst (Escat 103) was purchased from Engelhard Industries. 1-(3-Dimethylaminopropyl)-3-ethyl-carbodiimide (EDAC) was purchased from ACROS Organics. *N*-Iodosuccinimide (NIS) was freshly crystallized from $CCl_4$/dioxane. Silver trifluoromethanesulfonate (AgOTf) was purchased from Aldrich Chemical Co, and dried at 100 °C for 2 h before use. Rubber septa used to close reaction flasks containing organic solvents were protected with a thin Teflon™ sheet, to avoid leaching. Solutions in organic solvents were dried with anhydrous $Na_2SO_4$, and concentrated at 40 °C/2 kPa.

**General Procedure for Removal of the 2-*O*-Levulinoyl Group:** Hydrazine acetate (1.2 mmol) in MeOH (2 mL) was added to a mixture of 2-*O*-levulinoyl sugar (1 mmol) in $CH_2Cl_2$ (20 mL), and the mixture was stirred overnight at room temperature, when TLC showed that the reaction was complete. The mixture was concentrated, and the product was isolated by chromatography.

**General Procedure for Glycosylation with NIS/AgOTf**

**Procedure A:** Molecular sieves (4 Å, 0.5 g) were added to a stirred solution of the glycosyl acceptor (1 mmol) and thioglycoside glycosyl donor (1.2–1.3 mmol) in $CH_2Cl_2$ (10–15 mL). After 15–30 min, NIS (1.5 mmol) followed by solid AgOTf (0.5 mmol) was added. The mixture, which became red almost instantaneously, was stirred at room temperature (unless specified otherwise in Table 1) for 15–30 min, when TLC showed that the reaction was complete. After filtration through a celite pad into a separating funnel and partitioning of the filtrate between $CH_2Cl_2$ and aq $Na_2S_2O_3$/aq

$NaHCO_3$, the combined organic layers were dried, concentrated, and the residue was chromatographed.

**Procedure B:** Molecular sieves (4 Å, 0.5 g) were added to a stirred solution of the glycosyl acceptor (1 mmol) and the thioglycoside glycosyl donor (1.2–1.3 mmol) in ca. 7:1 toluene/$CH_2Cl_2$ (ca. 15 mL) under nitrogen (Table 1, footnote [c]). The mixture was brought to reflux, unless specified otherwise in Table 1, and a solid mixture of NIS (1.5 mmol) and AgOTf (0.5 mmol) was quickly added. The stirring was continued at the same temperature until TLC showed that the reaction was complete (~15–30 min). After cooling to room temperature, the product was isolated as described above.

**5-(Methoxycarbonyl)pentyl 3-*O*-Benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-2-*O*-levulinoyl-α-D-mannopyranoside (3). From Acetate 1:** Activated molecular sieves (1.25 g) were added to a stirred solution of 1-*O*-acetyl derivative **1**[12] (2.18 g, 3.76 mmol) and methyl 6-hydroxyhexanoate[36] (2.75 g, 18.80 mmol). After 30 min, $BF_3{\cdot}Et_2O$ (2.38 mL, 18.8 mmol) was added and the stirring was continued overnight, when TLC (2:1 hexane/acetone) showed that the reaction was complete and that one product was formed. The mixture was filtered, the filtrate was washed with iced aq. $NaHCO_3$, and the combined organic layers were concentrated. Chromatography of the residue (9:1→2:1 hexane/acetone) gave the linker-equipped mannoside **3** (2.20 g, 88%).

**From Thioglycoside 5:** Following procedure A for glycosylation, methyl 6-hydroxyhexanoate (TLC 2:1 hexane/acetone), afforded after chromatography products **3** and **2**.

**Compound 3:** (466 mg, 70%). $[\alpha]_D$ = +29 ($c$ = 0.8; $CHCl_3$). $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$ = 6.09 (d, $J_{NH,4}$ = 9.1 Hz, 1 H, NH), 5.34 (dd, $J_{1,2}$ = 1.9, $J_{2,3}$ = 3.2 Hz, 1 H, 2-H), 5.17 (dd, $J_{2',3'a}$ = 8.3, $J_{2',3'b}$ = 4.6 Hz, 1 H, 2′-H), 4.75 (d, 1 H, 1-H), 4.64, 4.35 (2d, $^2J$ = 11.7 Hz, 2 H, C$H_2$Ph), 4.17–4.13 (m, 1 H, 4′a-H), 4.08–4.04 (m, 1 H, 4′b-H), 3.97 (q, $J$ = 10.4 Hz, 1 H, 4-H), 3.83 (dd, $J_{3,4}$ = 10.6 Hz, 1 H, 3-H), 3.81–3.76 (m, 1 H, 5-H), 3.67–3.63 (m, 4 H, 1a"-H, incl. s, 3.66, $OCH_3$), 3.40, 3.39 (2t, $J$ = 6.0 Hz, 1 H, 1b"-H), 2.74–2.62 (m, 4 H, $CH_2CH_2$), 2.33 (t, $J$ = 7.5 Hz, 2 H, 5′′-H), 2.21–2.03 (m, 11 H, 3′a,b-H, incl. 3s, 2.17, 2.04, 2.03, 2$CH_3$CO, $CH_3$), 1.69–1.56 (m, 4 H, 2′′-H, 4′′-H), 1.44–1.35 (m, 2 H, 3′′-H), 1.21 (d, $J_{5,6}$ = 6.3 Hz, 3 H, 6-H) ppm. $^{13}C$ NMR (150 MHz, $CDCl_3$): $\delta$ = 206.29 ($CH_2CO$), 174.29 ($COOCH_3$), 171.94 ($CH_2COO$), 170.77 (NHCO), 169.60, 169.34 (2$CH_3CO$), 97.46 ($J_{C,H}$ = 169.5 Hz, C-1), 73.65 (C-3), 71.05 (C-2′), 70.57 (C$H_2$Ph), 67.42 (C-2), 67.38 (C-5), 67.26 (C-1′′), 59.91 (C-4′), 52.47 (C-4), 51.47 ($OCH_3$), 37.91 ($CH_2CO$), 33.83 (C-5′′), 30.86 (C-3′), 29.69 ($CH_3$), 28.66 ($CH_2COO$), 28.10 (C-2′′), 25.59 (C-3′′), 24.39 (C-4′′), 20.76, 20.68 (2$CH_3CO$), 17.90 (C-6) ppm. ESI-MS: $m/z$: 688.2945 ([M + Na]$^+$; calcd. 688.2922). $C_{28}H_{39}NO_{10}S$ (665.3): calcd. C 59.54, H 7.12, N 2.10; found C 59.43, H 7.28, N 2.07.

**Compound 2:** (133 mg, 20%). $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$ = 6.15 (d, $J_{NH,4}$ = 7.5 Hz, 1 H, NH), 5.60 (d, $J_{2,3}$ = 2.8 Hz, 1 H, 2-H), 5.13 (dd, $J_{2',3'a}$ = 7.7, $J_{2',3'b}$ = 4.6 Hz, 1 H, 2′-H), 4.66, 4.30 (2d, $^2J$ = 11.3 Hz, 2 H, C$H_2$Ph), 4.52 (s, 1 H, 1-H), 4.21–4.04 (m, 1 H, 4′a,b-H), 3.92–3.82 (m, 3-H, $J_{3,4}$ = 10.7 Hz, 3 H, 5-H, 1a"-H, incl. dd, 3.90), 3.67 (s, 3 H, $OCH_3$), 3.54–3.39 (m, 4-H, $J$ = 10.4 Hz, 2 H, 1b"-H, incl. q, 3.51), 2.80–2.66 (m, 4 H, $CH_2CH_2$), 2.34 (t, $J$ = 7.5 Hz, 2 H, 5′′-H), 2.21–2.04 (m, 11 H, 3′a,b-H, incl. 3s, 2.14, 2.06, 2.04, 2$CH_3CO$, $CH_3$), 1.70–1.56 (m, 4 H, 2′′-H, 4′′-H), 1.44–1.33 (m, 2 H, 3′′-H), 1.28 (d, $J_{5,6}$ = 6.1 Hz, 3 H, 6-H) ppm. $^{13}C$ NMR (150 MHz, $CDCl_3$): $\delta$ = 206.16 ($CH_2CO$), 174.39 ($COOCH_3$), 172.15 ($CH_2COO$), 170.80 (NHCO), 169.57, 169.45 (2$CH_3CO$), 98.52 ($J_{C,H}$ = 155 Hz, C-1), 74.48 (C-3), 70.91 (C-2′), 70.70 (C$H_2$Ph), 69.96 (C-5), 69.32 (C-1′′), 67.36 (C-2), 59.82 (C-4′), 54.38 (C-4), 51.25 ($OCH_3$), 37.99 ($CH_2CO$), 33.79 (C-5′′), 30.84 (C-3′), 29.70 ($CH_3$), 28.93 ($CH_2COO$), 28.05 (C-2′′), 25.33 (C-3′′), 24.50 (C-4′′), 20.63, 20.59 (2$CH_3CO$), 17.87 (C-6) ppm. ESI-MS: $m/z$: 688.2947 ([M + Na]$^+$; calcd. 688.2922).

**5-(Methoxycarbonyl)pentyl 3-*O*-Benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-α-D-mannopyranoside (4):** Following the general procedure for cleavage of Lev group and chromatography (4:1→3:2 hexane/acetone) afforded the amorphous compound **4** (555 mg, 98%). $[\alpha]_D$ = +7 ($c$ = 0.4; $CHCl_3$). $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$ = 6.24 (d, $J_{NH,4}$ = 9.2 Hz, 1 H, NH), 5.16 (dd, $J_{2',3'a}$ = 8.3, $J_{2',3'b}$ = 4.6 Hz, 1 H, 2′-H), 4.83 (d, $J_{1,2}$ = 1.7 Hz, 1 H, 1-H), 4.67, 4.51 (2d, $^2J$ = 11.8 Hz, 2 H, C$H_2$Ph), 4.18–4.14 (m, 1 H, 4′a-H), 4.10–4.06 (m, 1 H, 4′b-H), 4.03–3.98 (m, 4-H, $J$ = 10.1 Hz, 2 H, 2-H, incl. 4.01, q), 3.82–3.76 (m, 3-H, $J_{2,3}$ = 3.2, $J_{3,4}$ = 10.3 Hz, 2 H, 5-H, incl. dd, 3.78), 3.70–3.65 (m, 4 H, 1a′′-H, incl. 3.67, s, $OCH_3$), 3.41, 3.39 (2t, $J$ = 6.0 Hz, 1 H, 1b′′-H), 2.72 (br. s, 1 H, 2-OH), 2.33 (t, $J$ = 7.3 Hz, 5′′-H), 2.22–2.17 (m, 1 H, 3′a-H), 2.09–2.03 (m, 7 H, 3′b-H, incl. 2s, 2.06, 2.03, 2$CH_3CO$), 1.68–1.57 (m, 4 H, 2′′-H, 4′′-H), 1.43–1.35 (m, 2 H, H-3′′), 1.20 (d, $J_{5,6}$ = 6.3 Hz, 3 H, 6-H) ppm. $^{13}C$ NMR (150 MHz, $CDCl_3$): $\delta$ = 174.31 ($COOCH_3$), 170.82 (NHCO), 169.73, 169.38 (2$CH_3CO$), 98.96 (C-1), 76.08 (C-3), 71.09 (C-2′), 71.00 (C$H_2$Ph), 67.09 (C-1′′), 66.95 (C-2), 66.86 (C-5), 59.99 (C-4′), 52.00 (C-4), 51.48 ($OCH_3$), 33.87 (C-5′′), 30.84 (C-3′), 28.72 (C-2′′), 25.62 (C-3′′), 24.43 (C-4′′), 20.77, 20.67 (2$CH_3CO$), 17.80 (C-6) ppm. ESI-MS: $m/z$: 590.2577 ([M + Na]$^+$; calcd. 590.2601). $C_{28}H_{41}NO_{11}$ (567.6): calcd. C 59.25, H 7.28, N 2.47; found C 59.09, H 7.44, N 2.74.

**Ethyl 3-*O*-Benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-1-thio-α-D-mannopyranoside (6):** Compound **5**[12] was treated as described in the general procedure for removal of Lev group. Chromatography of the crude product with 2:1 hexane/acetone afforded pure **6** (445 mg, 92%); m.p. 88–89 °C (from EtOAc/$i$Pr$_2$O). $[\alpha]_{20}$ = +85.3 ($c$ = 0.5; $CHCl_3$). $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$ = 5.89 (d, $J_{NH,4}$ = 9.1 Hz, 1 H, NH), 5.34 (d, $J_{1,2}$ = 1.4 Hz, 1 H, 1-H), 5.17 (dd, $J_{2',3'a}$ = 8.1, $J_{2',3'b}$ = 4.7 Hz, 1 H, 2′-H), 4.65, 4.49 (2 d, $^2J$ = 11.8 Hz, 2 H, C$H_2$Ph), 4.19–4.15 (m, 1 H, 4′a-H), 4.13–4.06 (m, 3 H, H-5, H-2, 4′b-H), 4.01 (q, $J$ = 9.7 Hz, 1 H, H-4), 3.73 (dd, $J_{2,3}$ = 3.2, $J_{3,4}$ = 10.3 Hz, 1 H, 3-H), 2.75 (br. s, 1 H, 2-OH), 2.69–2.55 (m, 2 H, S$CH_2CH_3$), 2.24–2.17 (m, 1 H, 3′a-H), 2.09–2.04 (m, 7 H, 3′b-H, incl. 2s, 2.07, 2.05, 2$CH_3$CO), 1.29 (t, $J$ = 7.4 Hz, 3 H, $SCH_2CH_3$), 1.21 (d, $J_{5,6}$ = 6.2 Hz, 3 H, 6-H) ppm. $^{13}C$ NMR (150 MHz, $CDCl_3$): $\delta$ = 170.94 (NH$CO$), 169.73, 169.41 (2 $CH_3CO$), 83.08 (C-1), 76.10 (C-3), 71.13 (C-2′), 71.05 (C$H_2$Ph), 68.31 (C-2), 67.58 (C-5), 59.97 (C-4′), 52.37 (C-4), 30.89 (C-3′), 25.04 (S$CH_2CH_3$), 20.86, 20.81 (2 $CH_3$CO), 17.76 (C-6), 14.83 ($SCH_2CH_3$) ppm. ESI MS: $m/z$: 506.1825 ([M + Na]$^+$; calcd. 506.1834). $C_{23}H_{33}NO_8S$ (483.2): calcd. C 57.13, H 6.88, N 2.90; found C 56.85, H 6.86, N 2.87.

**3-*O*-Benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-2-*O*-levulinoyl-α-D-mannopyranosyl Chloride (7):** 0.1 M $Cl_2$/$CCl_4$ (20 mL, 2 mmol) was added to a solution of thioglycoside **5** (730 mg, 1.25 mmol) in $CH_2Cl_2$ (1 mL). The solution turned yellow and TLC (9:1 toluene/acetone) showed that the starting material had been consumed. The mixture was concentrated with co-evaporation of toluene, and the residue was chromatographed on dry silica gel to give the chloride **6** (625 mg, 89%); m.p. 104–105 °C (from $i$Pr$_2$O containing a few drops of EtOAc). $[\alpha]_D$ = +26 ($c$ = 0.6; $CHCl_3$). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 6.02 (d, $J_{1,2}$ = 1.8 Hz, 1 H, 1-H), 5.94 (d, $J_{NH,4}$ = 8.3 Hz, 1 H, NH), 5.48 (d, $J_{2,3}$ = 2.8 Hz, 1 H, H-2), 5.17 (dd, $J_{2',3'a}$ = 8.0, $J_{2',3'b}$ = 4.9 Hz, 1 H, 2′-H), 4.63, 4.37 (2d, $^2J$ = 12.0 Hz, 2 H, C$H_2$Ph), 4.21–3.94 (m, 4-H, $J_{3,4}$ =

10.1 Hz, 3-H; q, 3.99, $J$ = 10.4 Hz, 5 H, 4′a,b-H, H-5, incl. dd, 4.02), 2.84–2.56 (m, 4 H, $CH_2CH_2$), 2.23–2.00 (m, 11 H, 3′a,b-H, incl. 3s, 2.17, 2.08, 2.03, $2CH_3CO$, $CH_3$), 1.25 (d, $J_{5,6}$ = 5.8 Hz, 3 H, 6-H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 206.24 ($CH_2CO$), 171.62 ($CH_2COO$), 170.86 (NHCO), 169.58, 169.52 ($2CH_3CO$), 90.14 ($J_{C,H}$ = 183.8 Hz, C-1), 71.65 (C-3), 70.98 (C-2′), 70.80 ($CH_2Ph$), 70.57 (C-5), 69.40 (C-2), 59.83 (C-4′), 52.17 (C-4), 37.80 ($CH_2CO$), 30.80 (C-3′), 29.68 ($CH_3$), 27.90 ($CH_2COO$), 20.80, 20.74 ($2CH_3CO$), 17.54 (C-6) ppm. ESI-MS: *m/z*: 578.1752 ([M + Na]$^+$; calcd. 578.1769). $C_{26}H_{34}ClNO_{10}$ (555.2): calcd. C 56.16, H 6.16, N 2.52; found C 56.33, H 6.16, N 2.50.

**Ethyl 3-*O*-Benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-2-*O*-levulinoyl-α-D-mannopyranosyl-(1→2)-3-*O*-benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-1-thio-α-D-mannopyranoside (8)**

**From Glycosyl Chloride 6 and Alcohol 7:** A solution of the chloride **6** (130 mg, 0.23 mmol) was added dropwise to a mixture of the acceptor **7** (110 mg, 0.21 mmol), AgOTf (59 mg, 0.23 mmol), TMU (30 μL, 0.23 mmol) and molecular sieves (150 mg) in $CH_2Cl_2$ (3 mL) at –40 °C. The cooling was removed, and the mixture was stirred at room temperature. When TLC (2:1 hexane/acetone) showed the reaction to be complete (~2 h), the mixture was washed successively with 10% HCl and aq $NaHCO_3$, the combined organic layers were dried, concentrated, and the residue was chromatographed (9:1 → 8.5:1.5 toluene/acetone). First eluted was a compound which co-chromtographed with **5** (11 mg, 10%) whose NMR spectroscopic data showed it to be identical with **5**.

Next eluted was compound **8** (120 mg, 58%); m.p. 179–180 °C (from $iPr_2O$ containing a few drops of EtOAc). $[\alpha]_{20}$ = +2.5 ($c$ = 0.6; $CHCl_3$). $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ = 5.82 (d, $J_{NH,4}$ = 8.8 Hz, 1 H, $NH^I$), 5.80 (d, $J_{NH,4}$ = 9.2 Hz, 1 H, $NH^{II}$), 5.44 (dd, $J_{1,2}$ = 2.2, $J_{2,3}$ = 3.1 Hz, 1 H, $2^{II}$-H), 5.26 (d, $J_{1,2}$ = 1.6 Hz, 1 H, $1^I$-H), 5.19 (2dd, $J_{2',3'a}$ = 8.0, $J_{2',3'b}$ = 4.6 Hz, 2 H, 2×2′-H), 4.83 (d, 1 H, $1^{II}$-H), 4.63, 4.39 (2d, $^2J$ = 11.8 Hz, 2 H, C$H_2$Ph), 4.59, 4.47 (2d, $^2J$ = 11.9 Hz, 2 H, C$H_2$Ph), 4.21–4.13 (m, 2 H, 2×4′a-H), 4.11–4.03 (m, 4 H, 2×4′b-H, $4^{II}$-H, $5^I$-H), 4.00 (m, partially overlapped, 1 H, $2^I$-H), 3.98 (q, partially overlapped, $J$ = 10.1 Hz, $4^I$-H), 3.84–3.79 (m, $3^{II}$-H, $J_{3,4}$ = 10.6 Hz, 2 H, $5^{II}$-H, incl. dd, 3.81), 3.81 (dd, $J_{2,3}$ = 2.9, $J_{3,4}$ = 10.4 Hz, 1 H, $3^I$-H), 2.77–2.53 (m, 6 H, $CH_2CH_2$, SC$H_2$CH$_3$), 2.26–2.01 (m, 19 H, 2×3′a,b-H, incl. 5s, 2.16, 2.10, 2.09, 2.05, 2.03, $4CH_3CO$, $CH_3$), 1.27 (t, $J$ = 7.4 Hz, 3 H, $SCH_2CH_3$), 1.18, (d, $J_{5,6}$ = 6.1 Hz, 3 H, $6^I$-H), 1.17 (d, $J_{5,6}$ = 6.2 Hz, 3 H, $6^{II}$-H) ppm. $^{13}$C NMR (150 MHz, $CDCl_3$): $\delta$ = 206.34 ($CH_2CO$), 171.68 ($CH_2COO$), 170.86, 170.81 (2NHCO), 169.67, 169.64, 169.57, 169.44 ($4CH_3CO$), 99.72 ($J_{C,H}$ = 166.7 Hz, C-$1^{II}$), 83.56 ($J_{C,H}$ = 166.7 Hz, C-$1^I$), 76.72 (C-$2^I$), 75.40 (C-$3^I$), 73.14 (C-$3^{II}$), 71.34 ($CH_2Ph$), 71.25, 71.14 (2C-2′), 70.59 ($CH_2Ph$), 68.82 (C-$5^{II}$), 68.38 (C-$5^I$), 67.27 (C-$2^{II}$), 60.00, 59.96 (2C-4′), 52.86 (C-$4^I$), 51.95 (C-$4^{II}$), 38.01 ($CH_2CO$), 31.03, 30.92 (2C-3′), 29.73 ($CH_3$), 28.18 ($CH_2COO$), 25.73 ($SCH_2CH_3$), 20.85, 20.84, 20.82, 20.81 ($4CH_3CO$), 17.97 (2 C, C-$6^{I,II}$), 14.90 ($SCH_2CH_3$) ppm. ESI-MS: *m/z*: 1025.3972 ([M + Na]$^+$; calcd. 1025.3929). $C_{49}H_{66}N_2O_{18}S$ (1003.5): calcd. C 58.67, H 6.63, N 2.79; found C 58.59, H 6.67, N 2.81.

**By Levulinoylation of 15:** EDAC (1.23 g, 6.4 mmol) was added to a solution of the disaccharide **15** (1.93 g, 2.1 mmol) and levulinic acid (0.74 g, 6.4 mmol) in $CH_2Cl_2$ (10 mL), followed by 4-dimethylaminopyridine (0.78 g, 6.4 mmol). The mixture was stirred overnight, when TLC (2:1 hexane/acetone) showed that the reaction was complete. After concentration, the residue was chromatographed (4:1→2:1 hexane/acetone) to give **8** (2.05 g, 97%).

**3-*O*-Benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-2-*O*-levulinoyl-α-D-mannopyranosyl-(1→2)-3-*O*-benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-α-D-mannopyranosyl Chloride (9):** A solution of the thioglycoside **8** (980 mg, 0.98 mmol) in $CH_2Cl_2$ (2 mL) was treated with chlorine (0.1 M $Cl_2/CCl_4$, 12 mL), as described above for a similar conversion (TLC 1:4 hexane/EtOAc). Chromatography on a column of dry silica gel afforded chloride **9** (800 mg, 91%); m.p. 156–157 °C (from $iPrO_2$ containing a few drops of EtOAc). $[\alpha]_{20}$ = –1.5 ($c$ = 0.3; $CHCl_3$). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 6.18 (d, $J_{NH,4}$ = 8.3 Hz, 1 H, NH), 6.09 (2d, overlapped, 2 H, $J_{4,NH}$ = 8.9 Hz, NH; $J_{1,2}$ = 1.8 Hz, $1^I$-H), 5.42 (dd, $J_{2,3}$ = 2.5 Hz, 1 H, $2^{II}$-H), 5.22–5.16 (m, 2 H, 2×2′-H), 4.83 (d, 1 H, $J_{1,2}$ = 1.8 Hz, $1^{II}$-H), 4.63–4.37 (4d, $^2J$ = 11.7 Hz, 4 H, $2CH_2$Ph), 4.25–3.96 (m, 9 H, $2^I$-H, $3^I$-H, 2×4′a,b-H, $4^{I,II}$-H, $5^I$-H), 3.87–3.76 (m, 2 H, $5^{II}$-H, incl. dd, 3.84, $J_{3,4}$ = 10.5 Hz, $3^{II}$-H), 2.77–2.61 (m, 4 H, $CH_2CH_2$), 2.26–1.97 (m, 19 H, 2×3′a,b-H, incl. 5s, 2.17, 2.11, 2.09, 2.07, 2.04, $4CH_3CO$, $CH_3$), 1.22, (d, $J_{5,6}$ = 5.5 Hz, 3 H, $6^I$-H), 1.18 (d, $J_{5,6}$ = 6.2 Hz, 3 H, $6^{II}$-H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 206.43 ($CH_2CO$), 171.70 ($CH_2COO$), 170.96, 170.90 (2NHCO), 169.76, 169.70, 169.57, 169.60 (4 C, $4CH_3CO$), 99.61 ($J_{C,H}$ = 170.4 Hz, C-$1^{II}$), 91.63 ($J_{C,H}$ = 182.0 Hz, C-$1^I$), 77.30 (C-$2^I$), 73.16 (C-$3^I$), 72.74 (C-$3^{II}$), 71.60 ($CH_2Ph$), 71.08, 71.00 (2×C-2′), 70.73 (C-$5^I$), 70.49 ($CH_2Ph$), 68.76 (C-$5^{II}$), 67.04 (C-$2^{II}$), 59.93, 59.86 (2×C-4′), 52.10, 51.88 (C-$4^{I,II}$), 37.89 ($CH_2CO$), 30.88, 30.80 (2×C-3′), 29.73 ($CH_3$), 28.04 ($CH_2COO$), 20.84, 20.81 (4 C, $4CH_3CO$), 17.85 (C-$6^{II}$), 17.61 (C-$6^I$) ppm. ESI-MS: *m/z*: 999.3475 ([M + Na]$^+$; calcd. 999.3506). $C_{47}H_{61}ClN_2O_{18}$ (976.4): calcd. C 57.75, H 6.29, N 2.87; found C 57.50, H 6.31, N 2.91.

**5-(Methoxycarbonyl)pentyl 3-*O*-Benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-2-*O*-levulinoyl-α-D-mannopyranosyl-(1→2)-3-*O*-benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)- 4,6-Dideoxy-α-D-mannopyranoside (10):** Reaction of **4** (4.15 g, 7.31 mmol) and **5** (4.67 g, 8.04 mmol), according to procedure A for glycosylation (TLC 2:1 hexane/acetone) gave, after chromatography (4:1 toluene/acetone) first syrupy disaccharide **10** (6.30 g, 80%). $[\alpha]_{20}$ = –23 ($c$ = 0.8; $CHCl_3$). $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ = 6.16 (d, $J_{NH,4}$ = 9.1 Hz, 1 H, $NH^I$), 5.76 (d, $J_{NH,4}$ = 9.2 Hz, 1 H, $NH^{II}$), 5.49 (dd, $J_{1,2}$ = 2.1, $J_{2,3}$ = 2.9 Hz, 1 H, $2^{II}$-H), 5.21–5.18 (m, 2 H, 2×2′-H), 4.84 (d, 1 H, $1^{II}$-H), 4.72 (d, $J_{1,2}$ = 1.9 Hz, 1 H, $1^I$-H), 4.64, 4.39 (2d, $^2J$ = 11.8 Hz, 2 H, C$H_2$Ph), 4.62, 4.50 (2d, $^2J$ = 11.8 Hz, 2 H, C$H_2$Ph), 4.20–4.14 (m, 2 H, 2×4′a-H), 4.11–4.07 (m, 4 H, 2×4′b-H, incl. q, 4.04, $J$ = 10.4 Hz, $4^{II}$-H; q, 4.00, $J$ = 10.3 Hz, $4^I$-H), 3.88 (dd, $J_{2,3}$ = 2.7 Hz, 1 H, $2^I$-H), 3.81 (dd, $J_{3,4}$ = 10.6 Hz, 1 H, $3^I$-H), 3.77 (dd, $J_{3,4}$ = 10.7 Hz, 1 H, $3^{II}$-H), 3.75–3.71 (m, 2 H, $5^{I,II}$-H), 3.68 (s, 3 H, $OCH_3$), 3.65–3.61 (m, 1 H, 1a"-H), 3.36, 3.34 (2t, $J$ = 5.8 Hz, 1 H, 1b"-H), 2.78–2.60 (m, 4 H, $CH_2CH_2$), 2.34 (t, $J$ = 7.2 Hz, 2 H, 5′′-H), 2.28–2.00 (m, 19 H, 2×3′a,b-H, incl. 5s, 2.16, 2.10, 2.06, 2.05, 2.04, $4CH_3CO$, $CH_3$), 1.66–1.56 (m, 4 H, 2′′-H, 4′′-H), 1.44–1.34 (m, 2 H, 3′′-H), 1.19, 1.16 (2d, $J_{5,6}$ = 6.3 Hz, 6 H, $6^{I,II}$-H) ppm. $^{13}$C NMR (150 MHz, $CDCl_3$): $\delta$ = 206.34 ($CH_2CO$), 174.29 ($COOCH_3$), 171.50 ($CH_2COO$), 170.80, 170.77 (2NHCO), 169.68, 169.59, 169.46, 169.38 ($4CH_3CO$), 99.61 ($J_{C,H}$ = 160.4 Hz, C-$1^{II}$), 98.64 ($J_{C,H}$ = 160.4 Hz, C-$1^I$), 75.09 (C-$3^I$), 74.82 (C-$2^I$), 72.86 (C-$3^{II}$), 71.31 ($CH_2Ph$), 71.16, 70.97 (2×C-2′), 70.29 ($CH_2Ph$), 68.59, 67.63 (C-$5^{I,II}$), 67.15 (C-1′′), 67.00 (C-$2^{II}$), 59.90 (2 C, 2×C-4′), 52.38 (C-$4^I$), 51.66 (C-$4^{II}$), 51.49 ($OCH_3$), 37.93 ($CH_2CO$), 33.81 (C-5′′), 30.92, 30.76 (2×C-3′), 29.70 ($CH_3$), 28.64 ($CH_2COO$), 28.06 (C-2′′), 25.57 (C-3′′), 24.35 (C-4′′), 20.84, 20.77, 20.76, 20.69 ($4CH_3CO$), 17.97, 17.86 (C-$6^{I,II}$) ppm. ESI-MS: *m/z*: 1109.4673 ([M + Na]$^+$; calcd. 1109.4682). $C_{54}H_{74}N_2O_{21}$ (1086.5): calcd. C 59.66, H 6.86, N 2.57; found C 59.40, H 6.92, N 2.57.

Eluted next was compound **12** (440 mg, 6%): $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ = 6.55 (d, $J_{NH,4}$ = 8.5 Hz, 1 H, NH$^{I}$), 6.13 (d, $J_{NH,4}$ = 7.9 Hz, 1 H, NH$^{II}$), 5.68 (br. d, $J_{2,3}$ = 2.9 Hz, 1 H, 2$^{II}$-H), 5.15–5.12 (m, 2 H, 2×2′-H), 4.79 (d, $J_{1,2}$ = 1.6 Hz, 1 H, 1$^{I}$-H), 4.74, 4.31 (2d, $^2J$ = 10.7 Hz, 2 H, C$H_2$Ph), 4.70 (br. s, 1 H, 1$^{I}$-H), 4.66, 4.30 (2d, $^2J$ = 11.5 Hz, 2 H, C$H_2$Ph), 4.26 (dd, $J_{2,3}$ = 2.4 Hz, 1 H, 2$^{I}$-H), 4.18–4.01 (m, 4 H, 2×4′a,b-H), 4.00–3.96 (m, H-3$^{I}$, $J_{3,4}$ = 10.6 Hz, 2 H, 5$^{I}$-H, incl. dd, 3.99), 3.91 (dd, $J_{3,4}$ = 10.6 Hz, 1 H, 3$^{II}$-H), 3.88–3.84 (m, 1 H, 5$^{II}$-H), 3.73–3.64 (m, 5 H, 1a"-H, 4$^{I}$-H incl. s, 3.68, $OCH_3$), 3.52 (q, $J$ = 10.1 Hz, 4$^{II}$-H), 3.39, 3.37 (2t, $J$ = 6.1 Hz, 1 H, 1b"-H), 2.82–2.54 (m, 4 H, $CH_2CH_2$), 2.34 (t, $J$ = 7.2 Hz, 2 H, 5′′-H), 2.20–2.00 (m, 19 H, 2×3′a,b-H, incl. 5s, 2.06, 2.04, 2.02, 2.01, 2.00, 4$CH_3$CO, $CH_3$), 1.70–1.57 (m, 4 H, 2′′-H, 4′′-H), 1.45–1.35 (m, 2 H, 3′′-H), 1.22, 1.19 (2d, $J_{5,6}$ = 6.2 Hz, 6 H, 6$^{I,II}$-H) ppm. $^{13}$C NMR (150 MHz, $CDCl_3$): $\delta$ = 207.78 ($CH_2CO$), 174.22 ($COOCH_3$), 172.38 ($CH_2COO$), 170.83, 170.74 (2NHCO), 169.62, 169.51, 169.40, 169.11 (4$CH_3CO$), 98.85 ($J_{C,H}$ = 166.2 Hz, C-1$^{I}$), 95.81 ($J_{C,H}$ = 152.1 Hz, C-1$^{II}$), 73.89 (C-3$^{II}$), 73.40 (C-3$^{I}$), 70.99, 70.93 (2×C-2′), 70.37 ($CH_2$Ph), 69.94 (C-2$^{I}$), 69.89 (C-5$^{II}$), 69.75 ($CH_2$Ph), 67.06 (C-1′′), 67.00 (2 C, C-2$^{II}$,5$^{I}$), 59.96, 59.82 (2×C-4′), 54.43 (C-4$^{II}$), 53.02 (C-4$^{I}$), 51.46 ($OCH_3$), 37.96 ($CH_2$CO), 33.81 (C-5′′), 30.87, 30.77 (2×C-3′), 29.69 ($CH_3$), 28.80 ($CH_2$COO), 28.28 (C-2′′), 25.53 (C-3′′), 24.40 (C-4′′), 20.76, 20.75, 20.65, 20.58 (4$CH_3$CO), 17.91, 17.87 (C-6$^{I,II}$) ppm. ESI-MS: $m/z$: 1109.4662 ([M + Na]$^+$; calcd. 1109.4682).

**5-(Methoxycarbonyl)pentyl 3-*O*-Benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-α-D-mannopyranosyl-(1→2)-3-*O*-benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-α-D-mannopyranoside (11):** Applying the general procedure for cleavage of Lev group to **10** gave, after chromatography (3:1 toluene/acetone), the deprotected, amorphous disaccharide **11** (970 mg, 98%). $[\alpha]_{20}$ = –7 ($c$ = 6; $CHCl_3$). $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ = 6.17 (d, $J_{NH,4}$ = 9.4 Hz, 1 H, NH$^{I}$), 5.80 (d, $J_{NH,4}$ = 9.4 Hz, 1 H, NH$^{II}$), 5.21–5.17 (m, 2 H, 2×2′-H), 5.00 (d, $J_{1,2}$ = 1.7 Hz, 1 H, 1$^{II}$-H), 4.74 (d, $J_{1,2}$ = 1.9 Hz, 1 H, 1$^{I}$-H), 4.70, 4.49 (2d, $^2J$ = 11.9 Hz, 2 H, C$H_2$Ph), 4.64, 4.52 (2d, $^2J$ = 11.9 Hz, 2 H, C$H_2$Ph), 4.23–4.21 (m, 1 H, 2$^{II}$-H), 4.19–4.15 (m, 2 H, 2×4′a-H), 4.13–4.07 (m, 4$^{II,I}$-H, in that order, $J$ = 10.4 Hz, 4 H, 2×4′b-H, incl. 2q, 4.11), 3.98 (br. t, 1 H, 2$^{I}$-H), 3.77–3.66 (m, 3$^{II}$-H; s, 3.68, $OCH_3$, $J_{2,3}$ = 2.8 Hz, $J_{3,4}$ = 10.4 Hz, 3$^{I}$-H; dd, 3.71, $J_{2,3}$ = 3.2 Hz, $J_{3,4}$ = 10.4 Hz, 6 H, 5$^{I,II}$-H, incl. dd, 3.76), 3.66–3.62 (m, 1 H, 1a"-H), 3.38, 3.36 (2×t, $J$ = 5.8 Hz, 1 H, 1b"-H), 2.54 (br. s, 1 H, 2$^{II}$-OH), 2.34 (t, $J$ = 7.2 Hz, 2 H, 5′′-H), 2.25–2.04 (m, 16 H, 2×3′a,b-H, incl. 4s, 2.12, 2.08, 2.06, 2.04, 4$CH_3$CO), 1.70–1.55 (m, 4 H, 2′′-H, 4′′-H), 1.46–1.31 (m, 2 H, 3′′-H), 1.21 (d, $J_{5,6}$ = 6.3 Hz, 3 H, 6$^{II}$-H), 1.16 (d, $J_{5,6}$ = 6.3 Hz, 6 H, 6$^{I}$-H) ppm. $^{13}$C NMR (150 MHz, $CDCl_3$): $\delta$ = 174.37 ($COOCH_3$), 170.80 (2 C, 2NHCO), 169.72, 169.62, 169.46, 169.40 (4$CH_3CO$), 101.00 (C-1$^{II}$), 98.82 (C-1$^{I}$), 75.59 (C-3$^{I}$), 75.12 (C-3$^{II}$), 73.83 (C-2$^{I}$), 71.24 ($CH_2$Ph), 71.13, 70.99 (2×C-2′), 70.49 ($CH_2$Ph), 68.03, (C-5$^{I}$), 67.85 (C-5$^{II}$), 67.04 (C-1′′), 66.24 (C-2$^{II}$), 59.94, 59.26 (2×C-4′), 52.00 (C-4$^{I}$), 51.51 ($OCH_3$), 51.14 (C-4$^{II}$), 33.81 (C-5′′), 30.91, 30.81 (2×C-3′), 28.60 (C-2′′), 25.59 (C-3′′), 24.31 (C-4′′), 20.84, 20.78, 20.76, 20.67 (4$CH_3$CO), 17.95, 17.75 (C-6$^{I,II}$) ppm. ESI-MS: $m/z$: 1011.4345 ([M + Na]$^+$; calcd. 1011.4314). $C_{49}H_{68}N_2O_{19}$ (988.5): calcd. C 59.50, H 6.93, N 2.92; found C 59.35, H 6.96, N 2.79.

**Ethyl 3-*O*-Benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-α-D-mannopyranosyl-(1→2)-3-*O*-benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-1-thio-α-D-mannopyranoside (15):** Hydrogen sulfide was passed for 30 min at room temperature through a solution of azido sugar **13**[19] (1.74 g, 2.98 mmol) in 2:1 pyridine/$H_2O$ (100 mL) and kept overnight in a loosely closed vessel at 40 °C, when TLC (95:5 DCM/MeOH) showed the reaction to be complete. The mixture was concentrated and material in the residue was chromatographed (97:3→95:5 $CH_2Cl_2$/MeOH), to afford ethyl 4-amino-3-*O*-benzyl-4,6-dideoxy-α-D-mannopyranosyl-(1→2)-4-amino-3-*O*-benzyl-4,6-dideoxy-1-thio-α-D-mannopyranoside (**14**) (1.37 g, 88%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 5.29 (d, $J_{1,2}$ = 1.5 Hz, 1 H, 1$^{I}$-H), 5.00 (d, $J_{1,2}$ = 1.6 Hz, 1 H, 1$^{II}$-H), 4.71–4.45 (m, 4 H, 2C$H_2$Ph), 4.06 (br. s, 2 H, 2$^{I,II}$-H), 3.86–3.65 (m, 2 H, 5$^{I,II}$-H), 3.55, 3.46 (2dd, $J_{2,3}$ = 2.9, $J_{3,4}$ = 9.9 Hz, 2 H, 3$^{I,II}$-H), 2.89, 2.86 (2t, partially overlapped, $J$ = 10.1 Hz, H-4$^{I,II}$), 2.70–2.50 (m, 2 H, SC$H_2$CH$_3$), 1.28 (t, $J$ = 7.1 Hz, 3 H, SCH$_2$C$H_3$), 1.26, (2d, $J_{5,6}$ = 6.2 Hz, 6 H, 6$^{I,II}$-H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 101.29 (C-1$^{II}$), 83.87 (C-1$^{I}$), 80.03, 79.66 (C-3$^{I,II}$), 74.77 (C-2$^{I}$), 71.53, 71.24 (2$CH_2$Ph), 70.16, 69.70 (C-5$^{I,II}$), 66.45 (C-2$^{II}$), 54.05, 53.26 (C-4$^{I,II}$), 25.53 (S$CH_2$CH$_3$), 18.14, 18.00 (2 C, C-6$^{I,II}$), 15.01 (SCH$_2$$CH_3$) ppm. ESI-MS: $m/z$: 533.2681 ([M + 1]$^+$; calcd. 533.2685).

A solution of the foregoing diamino sugar **14** (1.33 g, 2.5 mmol) and 2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronic acid[13] (1.2 g, 6.25 mmol) in $CH_2Cl_2$ (20 mL) was treated with a suspension of EDAC (1.2 g, 6.25 mmol) in $CH_2Cl_2$ (10 mL). The mixture was stirred for 2 h, when TLC (97:3 $CH_2Cl_2$/MeOH) showed that the reaction was complete. Concentration and chromatography of the crude product (98:2 $CH_2Cl_2$/MeOH) gave the title compound **15** (2.13 g, 96%); m.p. 112–113 °C (from $i$-Pr$_2$O containing a few drops of EtOAc), $[\alpha]_D$ = +32 ($c$ = 0.2; $CHCl_3$). $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ = 5.85 (d, $J_{NH,4}$ = 9.0 Hz, 1 H, NH$^{II}$), 5.81 (d, $J_{NH,4}$ = 9.1 Hz, 1 H, NH$^{I}$), 5.28 (br. s, 1 H, 1$^{I}$-H), 5.21–5.19 (m, 2 H, 2×2′-H), 4.98 (br. s, 1 H, 1$^{II}$-H), 4.69, 4.53 (2d, $^2J$ = 11.8 Hz, 2 H, C$H_2$Ph), 4.62, 4.45 (2d, $^2J$ = 11.9 Hz, 2 H, C$H_2$Ph), 4.20–4.16 (m, 3 H, 2×4′a-H, 2$^{II}$), 4.12–4.07 (m, 5 H, 2×4′b-H, 4$^{I,II}$-H, 2$^{I}$-H), 4.00–3.98 (m, 1 H, 5$^{I}$-H), 3.82–3.80 (m, 1 H, 5$^{II}$-H), 3.75 (dd, $J_{2,3}$ = 3.0, $J_{3,4}$ = 10.5 Hz, 1 H, 3$^{II}$-H), 3.68 (dd, $J_{2,3}$ = 2.4, $J_{3,4}$ = 9.9 Hz, 1 H, 3$^{I}$-H), 2.66–2.55 (m, 2 H, SC$H_2$CH$_3$), 2.23–2.01 (m, 16 H, 2×3′a,b-H, incl. 3s, 2.11, 2.09, 2.05, 4$CH_3$CO), 1.28 (t, $J$ = 7.4 Hz, 3 H, SCH$_2$C$H_3$), 1.20 (d, $J_{5,6}$ = 5.9 Hz, 3 H, 6$^{I}$-H), 1.18 (d, $J_{5,6}$ = 6.1 Hz, 3 H, 6$^{II}$-H) ppm. $^{13}$C NMR (150 MHz, $CDCl_3$): $\delta$ = 170.87, 170.84 (2×NHCO), 169.68, 169.67, 169.52, 169.43 (4$CH_3CO$), 101.13 (C-1$^{II}$), 83.67 (C-1$^{I}$), 75.70 (C-3$^{I}$), 75.61 (C-2$^{I}$), 75.30 (C-3$^{II}$), 71.13, 71.05 (2×C-2′), 71.08, 70.71 (2$CH_2$Ph), 68.46 (C-5$^{I}$), 68.20 (C-5$^{II}$), 66.43 (C-2$^{II}$), 59.96, 59.91 (2×C-4′), 52.34 (C-4$^{I}$), 51.30 (C-4$^{II}$), 30.91, 30.83 (2×C-3′), 25.66 (S$CH_2$CH$_3$), 20.84, 20.81, 20.79 (4 C, 4$CH_3$CO), 17.87, 17.79 (C-6$^{I,II}$), 14.87 (SCH$_2$$CH_3$) ppm. ESI-MS: $m/z$: 927.3522 ([M + Na]$^+$; calcd. 927.3561). $C_{44}H_{60}N_2O_{16}S$ (904.5): calcd. C 58.39, H 6.68, N 3.10; found C 58.97, H 6.71, N 3.03.

**Ethyl 4-Azido-3-*O*-benzyl-4,6-dideoxy-2-*O*-methyl-α-D-mannopyranosyl-(1→2)-4-azido-3-*O*-benzyl-4,6-dideoxy-1-thio-α-D-mannopyranoside (16):** MeI (ca. 1 mL, 13.5 mmol) was added to a stirred mixture of disaccharide **13**[19] (5.9 g, 11.1 mmol) and powdered KOH (1.87 g, 33.3 mmol) in $Me_2SO$ (15 mL). After 1 h, TLC (6:1 hexane/acetone) showed absence of the starting material and formation of one product. $CH_2Cl_2$ (50 mL) was added, and the mixture was filtered into a separating funnel containing aq. 10% AcOH. After partitioning, the combined organic layers were concentrated, and chromatography of the residue (95:5 hexane/acetone) gave amorphous **16** (5.8 g, 97%), $[\alpha]_D$ = +150 ( $c$ = 0; $CHCl_3$). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 5.11 (d, $J_{1,2}$ = 1.2 Hz, 2 H, 1$^{I}$-H), 4.85 (d, $J_{1,2}$ = 1.6 Hz, 1 H, 1$^{II}$-H), 4.72, 4.67 (2d, $^2J$ = 11.7 Hz, 2 H, C$H_2$Ph), 4.69, 4.54 (2d, $^2J$ = 11.4 Hz, 2 H, C$H_2$Ph), 3.96 (dd, $J_{2,3}$ = 2.8 Hz, 1 H, 2$^{I}$-H), 3.87–3.77 (m, 1 H, 5$^{I}$-H), 3.70 (dd, $J_{2,3}$ = 3.1, $J_{3,4}$ = 9.6 Hz, 1 H, 3$^{II}$-H), 3.65 (dd, $J_{3,4}$ = 9.9 Hz, 1 H, 3$^{I}$-H), 3.58–3.43 (m, 4$^{II}$-H, $J$ = 10.2 Hz, 2 H, 5$^{II}$-H, incl. t, 3.48), 3.37 (dd, 1 H, 2$^{II}$-H), 3.27 (t, $J$ = 9.9 Hz, 4$^{I}$-H), 3.21 (s, 3 H, $OCH_3$),

2.66–2.48 (m, 2 H, SC$H_2$CH$_3$), 1.30–1.23 (m, 6$^{II}$-H, $J_{5,6}$ = 6.1 Hz, 6$^{I}$-H; d, 1.27, $J_{5,6}$ = 6.1 Hz, 9 H, SCH$_2$C$H_3$, incl. d, 1.29) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 99.11 (C-1$^{II}$), 83.41 (C-1$^{I}$), 78.49 (C-3$^{I}$), 77.40 (C-3$^{II}$), 76.57 (C-2$^{II}$), 75.54 (C-2$^{I}$), 72.34, 72.02 (2$C$H$_2$Ph), 67.79 (C-5$^{II}$), 67.42 (C-5$^{I}$), 64.56 (C-4$^{I}$), 64.02 (C-4$^{II}$), 58.86 (OCH$_3$), 25.46 (S$C$H$_2$CH$_3$), 18.43 (C-6$^{II}$), 18.39 (C-6$^{I}$), 14.81 (SCH$_2$$C$H$_3$) ppm. ESI-MS: $m/z$: 621.2503 ([M + Na]$^+$; calcd. 621.2471). $C_{29}H_{38}N_6O_6S$ (598.3): calcd. C 58.18, H 6.40, N 14.04; found C 58.27, H 6.56, N 14.03.

**Ethyl 3-*O*-Benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-2-*O*-methyl-α-D-mannopyranosyl-(1→2)-3-*O*-benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-1-thio-α-D-mannopyranoside (18):** Azido sugar **16** (5.7 g, 9.51 mmol) in 2:1 pyridine/$H_2O$ (300 mL) was treated with $H_2S$ as described for the preparation of **14**, and chromatography of the crude product (97:3→95:5 DCM/MeOH) afforded ethyl 4-amino-3-*O*-benzyl-4,6-dideoxy-2-*O*-methyl-α-D-mannopyranosyl-(1→2)-4-amino-3-*O*-benzyl-4,6-dideoxy-1-thio-α-D-mannopyranoside (**17**, 5.01 g, 97%). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 5.25 (d, $J_{1,2}$ = 1.5 Hz, 1 H, 1$^{I}$-H), 4.99 (d, $J_{1,2}$ = 1.8 Hz, 1 H, 1$^{II}$-H), 4.71–4.51 (m, 4 H, 2C$H_2$Ph), 4.08 (dd, $J_{2,3}$ = 2.5 Hz, 1 H, 2$^{I}$-H), 3.88–3.78 (m, 1 H, 5$^{I}$-H), 3.68–3.45 (m, 3$^{I}$-H, $J_{2,3}$ = 3.8, $J_{3,4}$ = 9.5 Hz, 3$^{II}$-H; dd, 3.47, $J_{3,4}$ = 9.9 Hz, 4 H, 5$^{II}$-H, 2$^{II}$-H, incl. dd, 3.55), 3.33 (s, 3 H, OCH$_3$), 2.93 (t, partially overlapped, $J$ = 9.5 Hz, 4$^{II}$-H), 2.88 (t, partially overlapped, $J$ = 9.8 Hz, 4$^{I}$-H), 2.70–2.50 (m, 2 H, SC$H_2$CH$_3$), 1.31–1.25 (m, 6$^{II}$-H, $J_{5,6}$ = 6.5 Hz, 6$^{I}$-H; d, 1.27, $J_{5,6}$ = 6.1 Hz, 9 H, SCH$_2$C$H_3$, incl. d, 1.29) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 98.21 (C-1$^{II}$), 83.79 (C-1$^{I}$), 80.29 (C-3$^{I}$), 78.97 (C-3$^{II}$), 75.71 (C-2$^{II}$), 74.22 (C-2$^{I}$), 71.64, 71.25 (2$C$H$_2$Ph), 70.31 (C-5$^{II}$), 70.06 (C-5$^{I}$), 58.85 (OCH$_3$), 54.07 (C-4$^{I}$), 53.47 (C-4$^{II}$), 25.36 (S$C$H$_2$CH$_3$), 18.03, 17.99 (C-6$^{I,II}$), 14.91 (SCH$_2$$C$H$_3$) ppm. ESI-MS: $m/z$: 547.2822 ([M + 1]$^+$; calcd. 527.2842).

A solution of the foregoing diamino sugar **17** (4.8 g, 8.78 mmol) and 2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronic acid[13] (4.5 g, 22 mmol) in $CH_2Cl_2$ (60 mL) was treated with EDAC (4.22 g, 22 mmol) as described for the preparation of **15**. After 2 h, when TLC (97:3 $CH_2Cl_2$/MeOH) showed that all starting material had been consumed, the mixture was concentrated, and chromatography (98:2 $CH_2Cl_2$/MeOH) gave the coupling product **18** (7.26 g, 90%); m.p. 173–174 °C (from $i$PrO$_2$ containing a few drops of EtOAc). [$\alpha$]$_D$ = –175 ($c$ = 0.2; $CHCl_3$). $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ = 5.86 (d, $J_{NH,4}$ = 9.3 Hz, 1 H, NH$^{II}$), 5.78 (d, $J_{NH,4}$ = 8.9 Hz, 1 H, NH$^{I}$), 5.24 (d, $J_{1,2}$ = 1.0 Hz, 1 H, 1$^{I}$-H), 5.22–5.20 (m, 2 H, 2×2′-H), 4.94 (d, $J_{1,2}$ = 1.5 Hz, 1 H, 1$^{II}$-H), 4.71–4.50 (m, 4 H, 2C$H_2$Ph), 4.22–4.06 (m, 7 H, 2×4′a,b-H, 4$^{II}$-H, 2 $^{I}$-H, 4$^{I}$-H, in that order), 4.04–3.99 (m, 1 H, 5$^{I}$-H), 3.80–3.74 (m, 3$^{II}$-H, $J_{2,3}$ = 2.8, $J_{3,4}$ = 10.9 Hz, 2 H, 5$^{II}$-H, incl. dd, 3.79), 3.71–3.69 (m, 3$^{I}$-H, $J_{2,3}$ = 2.5, $J_{3,4}$ = 10.4 Hz, 2 H, 2$^{II}$-H, incl. dd, 3.70), 3.32 (s, 3 H, OCH$_3$), 2.67–2.55 (m, 2 H, SC$H_2$CH$_3$), 2.28–2.02 (m, 16 H, 2×3′a,b-H, incl. 4s, 2.10, 2.09, 2.05, 2.04, 4CH$_3$CO), 1.28 (t, $J$ = 7.4 Hz, 3 H, SCH$_2$C$H_3$), 1.22 (d, $J_{5,6}$ = 6.2 Hz, 6$^{I}$-H), 1.18 (d, $J_{5,6}$ = 6.2 Hz, 6$^{II}$-H) ppm. $^{13}$C NMR (150 MHz, $CDCl_3$): $\delta$ = 99.70 (C-1$^{II}$), 83.75 (C-1$^{I}$), 76.26 (C-3$^{I}$), 75.38 (C-2$^{II}$), 75.17 (C-2$^{I}$), 74.83 (C-3$^{II}$), 71.41 (C$H_2$Ph), 71.20, 70.05 (2×C-2′), 70.49 (C$H_2$Ph), 68.84 (C-5$^{II}$), 68.37 (C-5$^{I}$), 59.97, 59.90 (2×C-4′), 58.85 (OCH$_3$), 52.85 (C-4$^{II}$), 51.96 (C-4$^{I}$), 30.93, 30.81 (2×C-3′), 25.62 (S$C$H$_2$CH$_3$), 20.87, 20.81, 20.78 (4 C, 4CH$_3$CO), 17.99 (C-6$^{II}$), 17.86 (C-6$^{I}$), 14.88 (SCH$_2$$C$H$_3$) ppm. ESI-MS: $m/z$: 941.3650 ([M + Na]$^+$; calcd. 941.3718). $C_{45}H_{62}N_2O_{16}S$ (918.4): calcd. C 58.88, H 6.80, N 3.05; found C 59.07, H 6.66, N 3.04.

**5-(Methoxycarbonyl)pentyl 3-*O*-Benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-2-*O*-methyl-α-D-mannopyranosyl-(1→2)-3-*O*-benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-α- (19) and β-D-Mannopyranoside (20):** Thioglycoside **18** (1.2 g, 1.3 mmol) and 5-(methoxycarbonyl)pentanol[36] (0.25 g, 1.7 mmol) were treated according to Procedure B to give, after chromatography 4:1 (toluene/acetone), first the α-linked product **19** (900 mg, 63%): [$\alpha$]$_D$ = –7 ($c$ = 0.8; $CHCl_3$). $^1$H NMR (60 MHz, $CDCl_3$): $\delta$ = 6.26 (d, $J_{NH,4}$ = 9.5 Hz, 1 H, NH$^{I}$), 5.73 (d, $J_{NH,4}$ = 9.1 Hz, 1 H, NH$^{II}$), 5.22–5.10 (m, 2 H, 2×2′-H), 4.97 (d, $J_{1,2}$ = 1.7 Hz, 1 H, 1$^{II}$-H), 4.72–4.50 (m, 1 H, 1$^{I}$-H, $J_{1,2}$ = 2.0 Hz, 5 H, 2C$H_2$Ph, incl. d, 4.71), 4.21–4.06 (m, 6 H, 2×4′a,b-H, 4$^{I,II}$-H), 4.00 (dd, $J_{2,3}$ = 2.5 Hz, 1 H, 2$^{I}$-H), 3.78 (dd, $J_{3,4}$ = 10.6 Hz, 3$^{I}$-H), 3.75–3.63 (m, 8 H, 2$^{II}$-H, 3$^{II}$-H, 5$^{I,II}$-H, 1′′a-H, incl. 3.67, s, 3 H, COOCH$_3$), 3.39, 3.37 (2t, $J$ = 5.7 Hz, 1 H, 1′′b-H), 3.27 (s, 3 H, 2$^{II}$-OCH$_3$), 2.34 (t, $J$ = 7.4 Hz, 2 H, 5′′-H), 2.27–2.02 (m, 16 H, 2×3′a,b-H, incl. 4s, 2.10, 2.05, 2.04, 2.02, 4CH$_3$CO), 1.73–1.55 (m, 4 H, 4′′-H, 2′′-H), 1.48–1.33 (m, 2 H, 3′′-H), 1.22 (d, $J_{5,6}$ = 6.2 Hz, 6$^{I}$-H), 1.16 (d, $J_{5,6}$ = 6.2 Hz, 6$^{II}$-H) ppm. $^{13}$C NMR (150 MHz, $CDCl_3$): $\delta$ = 174.45 ($C$OOCH$_3$), 170.82, 170.78 (2NHCO), 169.82, 169.53, 169.35, 169.29 (4CH$_3$$C$O), 99.59 ($J_{C,H}$ = 170.3 Hz, C-1$^{II}$), 98.91 ($J_{C,H}$ = 169.8 Hz, C-1$^{I}$), 76.20 (C-3$^{I}$), 75.17 (C-2$^{II}$), 74.67 (C-3$^{II}$), 73.51 (C-2$^{I}$), 71.64 (C$H_2$Ph), 71.22, 70.01 (2×C-2′), 70.26 (C$H_2$Ph), 68.70 (C-5$^{II}$), 68.76 (C-5$^{I}$), 66.96 (C-1′′), 59.97, 59.94 (2×C-4′), 58.85 (OCH$_3$-2$^{II}$), 52.17 (C-4$^{II}$), 51.78 (C-4$^{I}$), 51.54 (CO-OCH$_3$), 33.83 (C-5′′), 30.94, 30.81 (2×C-3′), 28.61 (C-2′′), 25.59 (C-3′′), 24.30 (C-4′′), 20.87, 20.78, 20.76, 20.65 (4CH$_3$CO), 17.94 (2 C, C-6$^{I,II}$) ppm. ESI-MS: $m/z$: 1025.4480 ([M + Na]$^+$; calcd. 1025.4447). $C_{50}H_{70}N_2O_{19}$ (1002.5): calcd. C 59.87, H 7.03, N 2.79; found C 59.70, H 7.21, N 2.86.

Eluted next was β-glycoside **20** (500 mg, 35%): $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ = 6.14 (d, $J_{NH,4}$ = 8.8 Hz, 1 H, NH$^{I}$), 5.92 (d, $J_{NH,4}$ = 9.5 Hz, 1 H, NH$^{II}$), 5.24 (dd, $J_{2',3'a}$ = 8.0, $J_{2',3'b}$ = 4.4 Hz, 1 H, 2′-H), 5.16 (dd, $J_{2',3'a}$ = 8.0, $J_{2',3'b}$ = 4.8 Hz, 1 H, 2′-H), 5.03 (d, $J_{1,2}$ = 1.7 Hz, 1 H, 1$^{II}$-H), 4.69, 4.51 (2d, $^2J$ = 12.0 Hz, 2 H, C$H_2$Ph), 4.66, 4.50 (2d, $^2J$ = 11.4 Hz, 2 H, C$H_2$Ph), 4.40 (d, $J_{1,2}$ = 0.7 Hz, 1 H, 1$^{I}$-H), 4.22 (dd, $J_{2,3}$ = 2.5 Hz, 2$^{I}$-H), 4.21–4.02 (m, 6 H, 2×4′a,b-H, 5$^{II}$-H, 4$^{II}$-H), 3.87–3.81 (m, 4$^{I}$-H, $J$ = 10.1 Hz, 2 H, 1′′a-H, incl. q, 3.84), 3.76 (dd, $J_{2,3}$ = 2.9, $J_{3,4}$ = 10.6 Hz, 1 H, 3$^{II}$-H), 3.74 (dd, 1 H, 2$^{II}$-H), 3.69 (dd, $J_{3,4}$ = 10.4 Hz, 1 H, 3$^{I}$-H), 3.65 (s, 3 H, COOCH$_3$), 3.46, 3.44 (2t, $J$ = 6.9 Hz, 1 H, 1′′b-H), 3.21 (s, 3 H, 2$^{II}$-OCH$_3$), 2.30 (t, $J$ = 7.4 Hz, 2 H, 5′′-H), 2.26–2.00 (m, 16 H, 2×3′a,b-H, incl. 4s, 2.10, 2.06, 2.04, 2.02, 4CH$_3$CO), 1.67–1.56 (m, 4 H, 4′′-H, 2′′-H), 1.41–1.33 (m, 2 H, 3′′-H), 1.28 (d, $J_{5,6}$ = 6.2 Hz, 6$^{I}$-H), 1.13 (d, $J_{5,6}$ = 6.2 Hz, 6$^{II}$-H) ppm. $^{13}$C NMR (150 MHz, $CDCl_3$): $\delta$ = 173.92 ($C$OOCH$_3$), 169.73, 169.42, 169.39, 169.26 (6 C, 2NHCO, 4CH$_3$$C$O), 100.05 ($J_{C,H}$ = 152.8 Hz, C-1$^{I}$), 99.79 ($J_{C,H}$ = 169.9 Hz, C-1$^{II}$), 78.20 (C-3$^{I}$), 75.47 (C-3$^{II}$), 75.30 (C-2$^{II}$), 72.41 (C-2$^{I}$), 71.75 (C$H_2$Ph), 71.10, 70.99 (2×C-2′), 70.94 (C-5$^{I}$), 70.23 (C$H_2$Ph), 69.82 (C-1′′), 68.01 (C-5$^{II}$), 59.97, 59.83 (2×C-4′), 58.77 (OCH$_3$-2$^{II}$), 53.32 (C-4$^{I}$), 51.57 (C-4$^{II}$), 51.41 (COO$C$H$_3$), 33.71 (C-5′′), 30.91, 30.74 (2×C-3′), 29.06 (C-2′′), 25.27 (C-3′′), 24.38 (C-4′′), 20.84, 20.75, 20.72, 20.62 (4CH$_3$CO), 17.92 (C-6$^{I}$), 17.71 (C-6$^{II}$) ppm. ESI-MS: $m/z$: 1025.4458 ([M + Na]$^+$; calcd. 1025.4447).

**5-(Methoxycarbonyl)pentyl 4-(3-Deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-2-*O*-methyl-α-D-mannopyranosyl-(1→2)-4-(3-deoxy-L-*glycero*-tetronamido)-4,6-Dideoxy-α-D-mannopyranoside (22):** A solution of **19** (1.15 g, 1.15 mmol) in MeOH (50 mL) was made strongly alkaline to litmus by addition of 0.1 M methanolic NaOMe and kept at room temperature overnight, when TLC (9:1 $CH_2Cl_2$/MeOH) showed the reaction to be complete. The mixture was neutralized with amberlite IR-120 (H$^+$-form), filtered, the filtrate was concentrated and chromatography of the residue (19:1 $CH_2Cl_2$/MeOH) gave the intermediate product, 5-(methoxycarbonyl)pentyl

3-*O*-benzyl-4-(3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-2-*O*-methyl-α-D-mannopyranosyl-(1→2)-3-*O*-benzyl-4-(3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-α-D-mannopyranoside **21** (855 mg, 90%): $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ = 7.06 (d, $J_{NH,4}$ = 9.6 Hz, 1 H, $NH^I$), 6.92 (d, $J_{NH,4}$ = 9.8 Hz, 1 H, $NH^{II}$), 5.05 (m, 1 H, 2′-H), 4.95–4.94 (m, 2 H, 2′-H, incl. 4.95, s, $1^{II}$-H), 4.73 (s, 1 H, $1^I$-H), 4.64, 4.50 (2d, $^2J$ = 11.8 Hz, 2 H, C$H_2$Ph), 4.59, 4.55 (2d, $^2J$ = 11.5 Hz, 2 H, C$H_2$Ph), 4.31 (m, 1 H, 4′a-H), 4.24 (m, 1 H, 4′a-H), 4.11–4.05 (m, 2 H, $4^{II}$-H, $4^I$-H, in that order), 3.95 (br. s, 1 H, $2^I$-H), 3.81–3.52 (m, 11 H, 2×4′b-H, $3^I$-H, $3^{II}$-H, $5^{II}$-H, $5^I$-H, $2^{II}$-H, 1′′a-H, in that order, incl. 3.65, s, $COOCH_3$), 3.37–3.34 (m, 1 H, 1′′b-H), 3.24 (s, 3 H, $2^{II}$-$OCH_3$), 2.32 (t, $J$ = 7.4 Hz, 2 H, 5′′-H), 2.07–1.99 (m, 2 H, 2×3′a-H), 1.81–1.79 (m 2 H, 2×3′b-H), 1.67–1.54 (m, 4 H, 4′′-H, 2′′-H), 1.43–1.30 (m, 2 H, 3′′-H), 1.21 (d, $J_{5,6}$ = 6.1 Hz, $6^I$-H), 1.16 (d, $J_{5,6}$ = 6.1 Hz, $6^{II}$-H) ppm. $^{13}$C NMR (150 MHz, $CDCl_3$): $\delta$ = 174.45, 174.70, 174.25 (*C*$OOCH_3$, 2NHCO), 99.34 (C-$1^{II}$), 98.71 (C-$1^I$), 76.25 (C-$3^I$), 75.52 (C-$3^{II}$), 75.48 (C-$2^{II}$), 74.04 (C-$2^I$), 71.89 (*C*$H_2$Ph), 71.34, (2 C, 2×C-2′), 70.85 (*C*$H_2$Ph), 68.56 (C-$5^{II}$), 68.78 (C-$5^I$), 67.17 (C-1′′), 60.16, 60.02 (2×C-4′), 58.79 ($OCH_3$-$2^{II}$), 51.96 (C-$4^I$), 51.49 ($COOCH_3$), 51.47 (C-$4^{II}$), 35.79, 35.67 (2×C-3′), 33.74 (C-5′′), 28.76 (C-2′′), 25.55 (C-3′′), 24.38 (C-4′′), 17.91, 17.87 (C-$6^{I,II}$) ppm. ESI-MS: *m*/*z*: 857.4017 ([M + Na]$^+$; calcd. 857.4048).

A mixture of the foregoing dibenzyl ether **21** (550 mg, 0.66 mmol) and Escat 103 (500 mg) in MeOH (15 mL) was stirred overnight under hydrogen, when TLC (85:15 $CH_2Cl_2$/MeOH) showed that the reaction was complete. The mixture was filtered through a celite pad, the filtrate was concentrated, and a solution of the residue was eluted from a small silica gel column (85:15 $CH_2Cl_2$/MeOH). Fractions containing the desired material were pooled and, after concentration, a solution the residue in deionized water was filtered through a syringe filter (0.45 μm porosity) and freeze-dried, to give the disaccharide **22**, which was obtained as a white amorphous solid (380 mg, 90%): $^1$H NMR (600 MHz, $D_2O$): $\delta$ = 5.17 (d, $J_{1,2}$ = 1.7 Hz, 1 H, $1^{II}$-H), 4.92 (d, $J_{1,2}$ = 1.6 Hz, 1 H, $1^I$-H), 4.30, 4.28 (2dd, $J_{2',3'a}$ = 8.8, $J_{2',3'b}$ = 4.7 Hz, 2 H, 2×2′-H), 4.09 (dd, $J_{2,3}$ = 3.4, $J_{3,4}$ = 10.7 Hz, 1 H, $3^{II}$-H), 4.06 (dd, $J_{2,3}$ = 3.2, $J_{3,4}$ = 10.3 Hz, 1 H, $3^I$-H), 3.96 (dd, 1 H, $2^I$-H), 3.94–3.82 (m, $4^{II}$-H, $J$ = 10.2 Hz, $4^I$-H; 3.84, t, $J$ = 10.5 Hz, 4 H, $5^{I,II}$-H, incl. 3.91, t), 3.77 (dd, 1 H, $2^{II}$-H), 3.75–3.73 (m, 4 H, 2×4′a,b-H), 3.71, 3.70 (2×t, $J$ = 6.2 Hz, 1′′a-H), 3.68 (s, 1 H, $COOCH_3$), 3.54, 3.53 (2t, $J$ = 6.2 Hz, 1′′b-H), 3.49 (s, 3 H, $2^{II}$-$OCH_3$), 2.40 (t, $J$ = 7.4 Hz, 2 H, 5′′-H), 2.06–2.00 (m, 2 H, 2×3′a-H), 1.88–1.83 (m, 2 H, 2×3′b-H), 1.65–1.59 (m, 4 H, 4′′-H, 2′′-H), 1.41–1.36 (m, 2 H, 3′′-H), 1.19 (d, $J_{5,6}$ = 6.0 Hz, $6^I$-H), 1.17 (d, $J_{5,6}$ = 6.2 Hz, $6^{II}$-H) ppm. $^{13}$C NMR (150 MHz, $D_2O$): $\delta$ = 180.32, 180.14, 180.02 (*C*$OOCH_3$, 2NHCO), 101.85 (C-$1^{II}$), 101.10 (C-$1^I$), 81.69 (C-$2^{II}$), 81.00 (C-$2^I$), 71.72, 71.70 (2×C-2′), 70.68 (C-1′′), 70.66 (C-$5^{II}$), 70.35 (C-$5^I$), 70.30 (C-$3^I$), 70.20 (C-$3^{II}$), 61.49 ($OCH_3$-$2^{II}$), 60.58 (2 C, 2×C-4′), 55.92 (C-$4^{II}$), 55.81 (C-$4^I$), 54.86 ($COOCH_3$), 38.72, 38.68 (2×C-3′), 36.34 (C-5′′), 30.81 (C-2′′), 27.60 (C-3′′), 27.33 (C-4′′), 19.60 (C-$6^{II}$), 19.54 (C-$6^I$) ppm. ESI-MS: *m*/*z*: 677.3000 ([M + Na]$^+$; calcd. 673.3109).

**5-(Methoxycarbonyl)pentyl 3-*O*-Benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-2-*O*-levulinoyl-α-D-mannopyranosyl-(1→2)-3-*O*-benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-α-D-mannopyranosyl-(1→2)-3-*O*-benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-α-D-mannopyranoside (23):** This compound was prepared from glycosyl donor **5** (153 mg, 0.26 mmol) and glycosyl acceptor **11** (220 mg, 0.22 mmol) according to procedure A for glycosylation (TLC 1:1 hexane/acetone). Chromatography (8:1 toluene/acetone) afforded the syrupy trisaccharide **23** (255 mg, 76%). $[\alpha]_D$ = –5.5 (*c* = 0.4; $CHCl_3$). $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ = 6.16 (d, $J_{NH,4}$ = 5.9 Hz, 1 H, $NH^{III}$), 5.93 (d, $J_{NH,4}$ = 9.7 Hz, 1 H, $NH^I$), $NH^{II}$ not observed, 5.41 (dd, $J_{1,2}$ = 1.9, $J_{2,3}$ = 2.6 Hz, 1 H, $2^{III}$-H), 5.22–5.16 (m, 3 H, 3×2′-H), 5.03 (br. s, 1 H, $1^{II}$-H), 4.72 (d, $J_{1,2}$ = 1.4 Hz, 1 H, $1^I$-H), 4.68–4.29 (m, 6 H, 3C$H_2$Ph), 4.22–3.98 (m, 10 H, 3×4′a,b-H, incl. $4^{II}$-H, $4^I$-H, $2^{II}$-H, $4^{III}$-H, in that order), 3.91 (m, 1 H, $2^I$-H), 3.78–3.62 (m, $3^I$-H; 3.67, s, $OCH_3$, $J_{2,3}$ = 3.1, $J_{3,4}$ = 10.4 Hz, $3^{III}$-H; dd, 3.77, $J_{2,3}$ = 3.1, $J_{3,4}$ = 10.4 Hz, $3^{II}$-H; dd, 3.73, $J_{2,3}$ = 2.6, $J_{3,4}$ = 10.7 Hz, 10 H, $5^{III}$-H, $5^{II}$-H, $5^I$-H, 1a"-H, in that order, incl. dd, 3.78), 3.37, 3.36 (2t, $J$ = 5.7 Hz, 1 H, 1b"-H), 2.76–2.61 (m, 4 H, $CH_2CH_2$), 2.33 (t, $J$ = 7.1 Hz, 2 H, 5′′-H), 2.28–2.00 (m, 27 H, 3×3′a,b-H, incl. 7s, 2.15, 2.14, 2.06, 2.05, 2.04, 2.02, 2.01, 6$CH_3CO$, $CH_3$), 1.70–1.52 (m, 4 H, 2′′-H, 4′′-H), 1.45–1.31 (m, 2 H, 3′′-H), 1.18 (d, $J_{5,6}$ = 6.2 Hz, 3 H, $6^{III}$-H), 1.15 (d, $J_{5,6}$ = 6.2 Hz, 3 H, $6^I$-H), 1.11 (d, $J_{5,6}$ = 6.2 Hz, 6 H, $6^{II}$-H) ppm. $^{13}$C NMR (150 MHz, $CDCl_3$): $\delta$ = 205.99 ($CH_2CO$), 174.18 (*C*$OOCH_3$), 171.28 ($CH_2COO$), 170.57, 170.51, 170.46 (3NHCO), 169.46, 169.42, 169.33, 169.25, 169.15 (6 C, 6$CH_3CO$), 100.57 ($J_{C,H}$ = 170.3 Hz, C-$1^{II}$), 98.88 ($J_{C,H}$ = 170.4 Hz, C-$1^I$), 98.15 ($J_{C,H}$ = 169.5 Hz, C-$1^{III}$), 75.31 (C-$3^{III}$), 74.67 (C-$2^I$), 73.99 (C-$2^{II}$), 73.75 (C-$3^{II}$), 73.23 (C-$3^I$), 71.25, (*C*$H_2$Ph), 71.21, 70.08, 70.01 (3×C-2′), 70.69, 70.47 (2×*C*$H_2$Ph), 68.74, 68.71 (C-$5^{II,III}$), 67.80 (C-$5^I$), 67.23 (C-$2^{III}$), 67.13 (C-1′′), 60.06, 59.94, 59.93 (3×C-4′), 52.12 (C-$4^I$), 51.76 (C-$4^{II}$), 51.65 (C-$4^{III}$), 51.58 ($OCH_3$), 38.00 (*C*$H_2$CO), 33.86 (C-5′′), 30.96, 30.85 (3 C, 3×C-3′), 29.75 ($CH_3$), 28.63 (*C*$H_2$COO), 28.13 (C-2′′), 25.62 (C-3′′), 24.35 (C-4′′), 20.94, 20.85, 20.81, 20.79, 20.69 (6 C, 6*C*$H_3$CO), 18.17 (C-$6^{II}$), 18.00 (C-$6^I$), 17.88 (C-$6^{III}$) ppm. ESI-MS: *m*/*z*: 1530.6467 ([M + Na]$^+$; calcd. 1530.6418). $C_{75}H_{101}N_3O_{29}$ (1506.7): calcd. C 59.87, H 6.94, N 2.76; found C 59.59, H 6.83, N 2.99.

**5-(Methoxycarbonyl)pentyl 3-*O*-Benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-2-*O*-levulinoyl-α-D-mannopyranosyl-(1→2)-bis[3-*O*-benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-α-D-mannopyranosyl]-3-*O*-benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-α-D-mannopyranoside (25)**

**From Disaccharide 11 and Chloride 9:** A mixture of acceptor **11** (160 mg, 0.16 mmol), donor **9** (203 mg, 0.21 mmol) and 4-Å MS (150 mg) in $CH_2Cl_2$ (3 mL) was stirred under nitrogen for 30 min. A solution of AgOTf (54 mg, 0.21 mmol) and 2,6-di-*tert*-butyl-4-methylpyridine (34 mg, 0.17 mmol) was added dropwise and the mixture was stirred for 2 h, when TLC (hexane/acetone, 1:1) showed the reaction to be complete. The mixture was filtered through a celite pad into a separating funnel and partitioned between $CH_2Cl_2$ and aq $Na_2S_2O_3$/aq $NaHCO_3$. The combined organic layers were dried, concentrated, and chromatography (4:1→3:2 hexane/acetone) gave a, 2:1 mixture of products **25** and **27**. Subsequent chromatography (98:2 toluene/MeOH) gave **25** (113 mg, 35%) and **27** (60 mg, 18%).

**Compound 25:** $[\alpha]_D$ = –28 (*c* = 0.2; $CHCl_3$). $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ = 6.15 (d, $J_{NH,4}$ = 9.4 Hz, 1 H, $NH^I$), 5.90 (br. s, 2 H, $NH^{III,IV}$), 5.72 (br. s, 1 H, $NH^{II}$), 5.43 (dd, $J_{1,2}$ = 2.3, $J_{2,3}$ = 2.5 Hz, 1 H, $2^{IV}$-H), 5.21–5.15 (m, 4 H, 4×2′-H), 5.03 (d, $J_{1,2}$ = 2.4 Hz, 1 H, $1^{III}$-H), 4.98 (br. s, 1 H, $1^{II}$-H), 4.74 (br. s, 1 H, $1^{IV}$-H), 4.71 (d, $J_{1,2}$ = 1.6 Hz, 1 H, $1^I$-H), 4.66–4.29 (m, 8 H, 4C$H_2$Ph), 4.20–4.00 (m, $4^{IV}$-H, $J$ = 10.1 Hz, 12 H, 4×4′a,b-H, $4^I$-H, $2^{II,III}$-H, incl. q, 4.01), 3.90 (br. s, 1 H, $2^I$-H), 3.78–3.72 (m, $3^{I,II}$-H, $J_{2,3}$ = 2.4, $J_{3,4}$ = 10.3 Hz, $3^{III,IV}$-H; dd, 3.74, $J_{2,3}$ = 2.4, $J_{3,4}$ = 10.6 Hz, 5 H, $5^{IV}$-H, incl. dd, 3.77), 3.71–3.61 (m, 7 H, $5^{I–III}$-H, 1a"-H, incl. 3.68, s, $OCH_3$), 3.37, 3.35 (2t, $J$ = 5.9 Hz, 1 H, 1b"-H), 2.71–2.60 (m, 4 H, $CH_2CH_2$), 2.32 (t, $J$ = 7.1 Hz, 2 H, 5′′-H), 2.25–2.00 (m, 35 H, 4×3′a,b-H, incl. 9s, 2.14, 2.10, 2.09, 2.06, 2.05, 2.04, 2.03, 2.02,

2.01, 8$CH_3CO$, $CH_3$), 1.70–1.54 (m, 4 H, 2′′-H, 4′′-H), 1.45–1.30 (m, 2 H, 3′′-H), 1.18 (d, $J_{5,6}$ = 6.3 Hz, 3 H, $6^{I}$-H), 1.16 (d, $J_{5,6}$ = 6.2 Hz, 3 H, $6^{II}$-H), 1.12 (d, $J_{5,6}$ = 6.1 Hz, 3 H, $6^{IV}$-H), 1.11 (d, $J_{5,6}$ = 6.1 Hz, 3 H, $6^{III}$-H) ppm. $^{13}$C NMR (150 MHz, $CDCl_3$): $\delta$ = 205.95 ($CH_2CO$), 174.13 ($COOCH_3$), 171.19 ($CH_2COO$), 170.48, 169.40, 169.34, 169.26 (12 C, 4NHCO, 8$CH_3CO$), 100.96 ($J_{C,H}$ = 176.5 Hz, C-$1^{III}$), 99.90 (br. s, $J_{C,H}$ = 173.1 Hz, C-$1^{II}$), 98.73 ($J_{C,H}$ = 167.3 Hz, C-$1^{I}$), 98.48 ($J_{C,H}$ = 173.7 Hz, C-$1^{IV}$), 75.03, 74.33 (C-$3^{I,II}$), 74.52 (C-$2^{I}$), 74.11, 73.52 (C-$3^{III,IV}$), 73.67 (C-$2^{III}$), 73.10 (C-$2^{II}$), 71.11 (C-2′), 71.06 ($CH_2Ph$), 71.04, 71.02, 70.91 (3 × C-2′), 70.86, 70.47 (3 C, 3$CH_2Ph$), 68.87, 67.85 (C-$5^{II,III}$), 67.82 (C-$5^{IV}$), 67.22 (C-$2^{IV}$), 67.07 (C-1′′), 59.96, 59.91, 59.87 (4 C, 4 × C-4′), 51.97, 51.82, 51.71, 51.59 (C-$4^{I–IV}$), 51.52 ($OCH_3$), 37.97 ($CH_2CO$), 33.79 (C-5′′), 30.93, 30.88, 30.83 (4 C, 4 × C-3′), 29.69 ($CH_3$), 28.57 (C-2′′), 28.10 ($CH_2COO$), 25.59 (C-3′′), 24.27 (C-4′′), 20.82, 20.80, 20.77, 20.75, 20.74, 20.69, 20.65 (8 C, 8$CH_3CO$), 18.11, 18.07, 17.98, 17.86 (C-$6^{I–IV}$) ppm. ESI-MS: *m/z*: 1951.8168 ([M + Na]$^+$; calcd. 1951.8155). $C_{96}H_{128}N_4O_{37}$ (1928.8): calcd. C 59.74, H 6.68, N 2.90; found C 59.94, H 6.87, N 2.94.

**Compound 27:** $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ = 7.73 (br. s 1 H, $NH^{IV}$), 6.38 (d, $J_{NH,4}$ = 9.4 Hz, 1 H, $NH^{I}$), 6.30 (br. s 1 H, $NH^{III}$), 6.12 (d, $J_{NH,4}$ = 9.7 Hz, 1 H, $NH^{II}$), 5.49 (dd, $J_{1,2}$ = 1.4, $J_{2,3}$ = 3.0 Hz, 1 H, $2^{IV}$-H), 5.38 (br. s, 1 H, $1^{IV}$-H), 5.30–5.14 (m, 4 H, 4 × 2′-H), 4.97 (d, $J_{1,2}$ = 2.2 Hz, 1 H, $1^{II}$-H), 4.85–4.44 (m, $1^{I}$-H, $J_{1,2}$ = 1.7 Hz, 6 H, 5C*H*Ph, incl. d, 4.76), 4.34–4.28 (m, 4 H, 2C*H*Ph, incl. br. s, 4.34, $1^{III}$-H; br. s, 4.33, $2^{II}$-H), 4.24 (q, $J$ = 10.1 Hz, $4^{IV}$-H), 4.20–3.97 (m, $4^{II}$-H, $J$ = 9.9 Hz, 11 H, $5^{IV}$-H, 4 × 4′a-H, 3 × 4′b-H, $4^{I}$-H, $2^{III}$-H, 1a"-H, incl. br. s, 4.06, $2^{I}$-H; q, 3.99), 3.85 (dd, $J_{2,3}$ = 3.2, $J_{3,4}$ = 10.8 Hz, 1 H, $3^{IV}$-H), 3.82 (dd, $J_{2,3}$ = 2.7, $J_{3,4}$ = 9.9 Hz, 1 H, $3^{I}$-H), 3.79–3.65 (m, 1 H, $3^{II}$-H; 3.69, s, $OCH_3$, $J_{2,3}$ = 3.2, $J_{3,4}$ = 10.8 Hz, 9 H, 4′b-H, $3^{III}$-H, $5^{I–III}$-H, incl. dd, 3.71), 3.59 (q, $J$ = 9.7 Hz, 1 H, $4^{III}$-H), 3.41, 3.39 (2t, $J$ = 5.6 Hz, 1 H, 1b"-H), 2.61–2.55 (m, 4 H, $CH_2CH_2$), 2.36 (t, $J$ = 7.1 Hz, 2 H, 5′′-H), 2.35–1.82 (m, 35 H, 4 × 3′a,b-H, incl. 9s, 2.08, 2.07, 2.06, 2.04, 2.03, 2.01, 1.99, 1.96, 8$CH_3CO$, $CH_3$), 1.77–1.58 (m, 4 H, 2′′-H, 4′′-H), 1.55–1.36 (m, 2 H, 3′′-H), 1.26 (d, $J_{5,6}$ = 6.2 Hz, 3 H, $6^{IV}$-H), 1.22 (d, $J_{5,6}$ = 6.3 Hz, 3 H, $6^{I}$-H), 1.14 (d, $J_{5,6}$ = 6.2 Hz, 3 H, $6^{II}$-H), 1.09 (d, $J_{5,6}$ = 6.1 Hz, 3 H, $6^{I}$-H) ppm. $^{13}$C NMR (150 MHz, $CDCl_3$): $\delta$ = 206.36 ($CH_2CO$), 174.35 ($COOCH_3$), 171.55 ($CH_2COO$), 170.61, 170.51, 170.08, 170.00, 169.67, 169.54, 169.36, 169.31, 169.27 (12 C, 4NHCO, 8$CH_3CO$), 99.80 ($J_{C,H}$ = 171.8 Hz, C-$1^{II}$), 98.87 ($J_{C,H}$ = 169.6 Hz, C-$1^{I}$), 97.51 ($J_{C,H}$ = 158.5 Hz, C-$1^{III}$), 97.07 ($J_{C,H}$ = 174.9 Hz, C-$1^{IV}$), 77.96 (C-$3^{III}$), 76.26 (C-$3^{I}$), 74.98 (C-$3^{IV}$), 73.85 (br. s, C-$3^{I}$), 73.30 (C-$2^{I}$), 71.71 ($CH_2Ph$), 71.24, 71.20 (2 × C-2′), 71.06 ($CH_2Ph$), 71.00, 70.57 (2 × C-2′), 70.31 (C-$2^{II}$), 69.96 (C-$5^{III}$), 69.50 ($CH_2Ph$), 69.10 (C-$5^{IV}$), 68.28 (C-$2^{IV}$), 67.88 (C-$5^{I}$), 67.71 (C-$2^{III}$), 67.00 (C-1′′), 60.47, 59.93, 59.90, 59.68 (4 × C-4′), 54.19 (C-$4^{III}$), 52.32 (C-$4^{II}$), 52.16 (C-$4^{I}$), 51.61 (C-$4^{IV}$), 51.55 ($OCH_3$), 38.15 ($CH_2CO$), 33.81 (C-5′′), 30.97, 30.79. 30.48 (4 C, 3 × C-3′), 29.57 ($CH_3$), 28.55 (C-2′′), 28.27 ($CH_2COO$), 25.57 (C-3′′), 24.24 (C-4′′), 20.77, 20.73, 20.71, 20.66, 20.60 (8 C, 6$CH_3CO$), 18.24 (C-$6^{II}$), 18.00, 17.90 (C-$6^{I,IV}$), 17.65 (C-$6^{III}$) ppm. ESI-MS: *m/z*: 1967.7856 ([M + K]$^+$; calcd. 1967.7895).

**From Trisaccharide 23:** Trisaccharide **23** (200 mg, 0.13 mmol) was treated with $NH_2NH_2$·AcOH (14 mg, 0.16 mmol), as described in the general procedure for removal of the Lev group. Chromatography (99.5:0.5→97:3 $CH_2Cl_2$/MeOH), gave 5-(methoxycarbonyl) pentyl 3-*O*-benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-2-*O*-levulinoyl-*α*-D-mannopyranosyl-(1→2)-3-*O*-benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-*α*-D-mannopyranosyl-(1→2)-3-*O*-benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-*α*-D-mannopyranoside (**24**) in virtually theoretical yield (ca. 180 mg): $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ = 6.20 (d, $J_{NH,4}$ = 8.5 Hz, 1 H, $NH^{I}$), 5.81 (d, $J_{NH,4}$ = 8.0 Hz, 1 H, $NH^{II}$), $NH^{III}$ not observed, 5.22–5.16 (m, 3 H, 3 × 2′-H), 5.06 (d, $J_{1,2}$ = 2.4 Hz, 1 H, $1^{II}$-H), 4.87 (br. s, 1 H, $1^{III}$-H), 4.73 (d, $J_{1,2}$ = 1.9 Hz, 1 H, $1^{I}$-H), 4.66–4.43 (m, 6 H, 3C$H_2$Ph), 4.20–4.03 (m, 11 H, 3 × 4′a,b-H, $4^{II}$-H, $4^{I}$-H, $2^{II}$-H, $4^{III}$-H, $2^{III}$-H in that order), 3.93 (m, 1 H, $2^{I}$-H), 3.80–3.62 (m, $3^{III}$-H; 3.67, s, $OCH_3$, $J_{2,3}$ = 2.8, $J_{3,4}$ = 8.5 Hz, $3^{II}$-H; dd, 3.74, $J_{2,3}$ = 3.1, $J_{3,4}$ = 8.5 Hz, $3^{I}$-H; dd, 3.72, $J_{2,3}$ = 3.0, $J_{3,4}$ = 9.1 Hz, 10 H, $5^{III}$-H, $5^{II}$-H, $5^{I}$-H, 1a"-H, in that order, incl. 3.76), 3.38, 3.36 (2t, $J$ = 5.7 Hz, 1 H, 1b"-H), 2.45 (br. s, 1 H, $2^{III}$-OH), 2.33 (t, $J$ = 7.2 Hz, 2 H, 5′′-H), 2.27–2.00 (m, 24 H, 3 × 3′a,b-H, incl. 6s, 2.14, 2.07, 2.05, 2.04, 2.02, 2.01, 6$CH_3CO$), 1.71–1.54 (m, 4 H, 2′′-H, 4′′-H), 1.46–1.31 (m, 2 H, 3′′-H), 1.19 (d, partially overlapped, $J_{5,6}$ = 6.3 Hz, 3 H, $6^{I}$-H), 1.18 (d, partially overlapped, $J_{5,6}$ = 6.6 Hz, 6 H, $6^{II}$-H), 1.12 (d, $J_{5,6}$ = 6.2 Hz, 6 H, $6^{III}$-H) ppm. $^{13}$C NMR (150 MHz, $CDCl_3$): $\delta$ = 174.47 ($COOCH_3$), 170.85, 170.83, 170.82 (3NHCO), 169.74, 169.72, 169.63, 169.62, 169.57 (6 C, 6$CH_3CO$), 100.74 (C-$1^{II}$), 99.80 (C-$1^{III}$), 98.89 (C-$1^{I}$), 75.57 (C-$3^{III}$), 75.23 (C-$3^{I}$), 74.23 (2 C, C-$3^{II}$, C-$2^{I}$), 73.13 (C-$2^{II}$), 71.16, ($CH_2Ph$), 71.15, 70.02, 70.99 (3 × C-2′), 70.84, 70.66 (2$CH_2Ph$), 68.75 (C-$5^{II}$), 68.14 (C-$5^{III}$), 67.79 (C-$5^{I}$), 67.06 (C-1′′), 66.64 (C-$2^{III}$), 60.03, 59.89 (3 C, 3 × C-4′), 52.05 (C-$4^{I}$), 51.71 (C-$4^{II}$), 51.52 ($OCH_3$), 51.22 (C-$4^{III}$), 33.81 (C-5′′), 30.94, 30.92, 30.83 (3 × C-3′), 28.57 (C-2′′), 25.57 (C-3′′), 24.27 (C-4′′), 20.86, 20.78, 20.76, 20.74, 20.64 (6 C, 6$CH_3CO$), 18.19 (C-$6^{II}$), 17.96 (C-$6^{I}$), 17.74 (C-$6^{III}$) ppm. ESI-MS: *m/z*: 1432.5818 ([M + Na]$^+$; calcd. 1432.6051).

The foregoing trisaccharide **24** (110 mg, 0.08 mmol) was treated with **5** following procedure A for glycosylation, and chromatography (99:1→95:5 toluene/MeOH) gave compounds **25** (124 mg, 81%) and **27** (25 mg, 16%).

**From Disaccharide 11 and Thioglycoside 8:** The disaccharide acceptor **11** was treated with the donor **8** according to procedure B (TLC 1:1 hexane/acetone). Chromatography with 4:1→3:2 hexane/acetone gave a mixture 5:1 of compounds **25** and **27**, which could be resolved by chromatography with 98:2 toluene/MeOH, affording amorphous **25** (1.49 g, 77%) and **27** (309 mg, 16%).

**5-(Methoxycarbonyl)pentyl 3-*O*-Benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-α-D-mannopyranosyl-(1→2)-bis[3-*O*-benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-α-D-mannopyranosyl]-3-*O*-benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-α-D-mannopyranoside (26):** When applied to compound **25** (1.49 g, 0.77 mmol), the general procedure for cleavage of Lev group gave, after chromatography (99.5:0.5 → 95:5 $CH_2Cl_2$/MeOH), product **26** in virtually theoretical yield as a foam (~1.40 g). $[\alpha]_D$ = –27 ($c$ = 0.2; $CHCl_3$). $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ = 6.20 (br. s, 1 H, $NH^{I}$), 5.80 (br. s, 1 H, NH), 5.21–5.15 (m, 4 H, 4 × 2′-H), 5.05 (d, $J_{1,2}$ = 2.5 Hz, 1 H, $1^{III}$-H), 4.99 (br. s, 1 H, $1^{II}$-H), 4.92 (br. s, 1 H, $1^{IV}$-H), 4.72 (d, $J_{1,2}$ = 1.7 Hz, 1 H, $1^{I}$-H), 4.66–4.44 (m, 8 H, 4C$H_2$Ph), 4.20–4.00 (m, 15 H, 4 × 4′a,b-H, $2^{II–IV}$-H, $4^{I–IV}$-H), 3.90 (br. s, 1 H, $2^{I}$-H), 3.80–3.72 (m, $3^{I,IV}$-H, $J_{2,3}$ = 2.8, $J_{3,4}$ = 9.4 Hz, $3^{II,III}$-H; dd, 3.74, $J_{2,3}$ = 3.0, $J_{3,4}$ = 10.6 Hz, 5 H, $5^{I}$-H, incl. dd, 3.78), 3.71–3.61 (m, 7 H, $5^{II,IV}$-H, 1a"-H, incl. 3.67, s, $OCH_3$), 3.37, 3.36 (2t, $J$ = 5.8 Hz, 1 H, 1b"-H), 2.45 (br. s, 1 H, $2^{IV}$-H), 2.34 (t, $J$ = 7.1 Hz, 2 H, 5′′-H), 2.22–2.00 (m, 35 H, 4 × 3′a,b-H, incl. 7s, 2.12, 2.09, 2.08, 2.05, 2.04, 2.03, 2.02, 2.01, 8$CH_3CO$), 1.70–1.54 (m, 4 H, 2′′-H, 4′′-H), 1.46–1.30 (m, 2 H, 3′′-H), 1.18 (d, $J_{5,6}$ = 6.2 Hz, 3 H, $6^{I}$-H), 1.17 (d, $J_{5,6}$ = 6.2 Hz, 3 H, $6^{II}$-H), 1.13 (d, partially overlapped, $J_{5,6}$ = 6.2 Hz, 3 H, $6^{IV}$-H), 1.12 (d, partially overlapped, $J_{5,6}$ = 6.2 Hz, 3 H, $6^{III}$-H) ppm. $^{13}$C NMR (150 MHz, $CDCl_3$): $\delta$ = 174.43 ($COOCH_3$), 170.75, 170.75 (4 C, 2NHCO), 169.71, 169.70, 169.59, 169.55 (8 C,

8$CH_3CO$), 100.74 (C-$1^{II}$), 99.95 (br. s, 2 C, C-$1^{III,IV}$), 98.74 (C-$1^{I}$), 75.67, 75.11 (C-$3^{I,IV}$), 75.59, 74.17 (br. s, 3 C, C-$2^{I}$, C-$3^{II,III}$), 73.06 (2 C, C-$2^{II,III}$), 71.14, 71.10, 71.03, 71.00, 70.95, 70.83, 70.76 (8 C, 4×C-2′, 4$CH_2$Ph), 68.95, 68.87 (C-$5^{II,III}$), 68.12 (C-$5^{IV}$), 67.80 (C-$5^{I}$), 67.06 (C-1′′), 66.60 (C-$2^{IV}$), 60.02, 59.96, 59.90, 59.89 (4 C, 4×C-4′), 51.97 (C-$4^{I}$), 51.66 (2 C, C-$4^{II,IV}$), 51.52 ($OCH_3$), 51.22 (C-$4^{III}$), 37.97 ($CH_2CO$), 33.79 (C-5′′), 30.93, 30.90. 30.81 (4 C, 4×C-3′), 28.55 (C-2′′), 25.57 (C-3′′), 24.25 (C-4′′), 20.82, 20.77, 20.76, 20.75, 20.69, 20.63 (8 C, 8$CH_3CO$), 18.09 (2 C, C-$6^{II,III}$), 17.97 (C-$6^{I}$), 17.76 (C-$6^{IV}$) ppm. ESI-MS: *m*/*z*: 1853.7856 ([M + Na]$^+$; calcd. 1853.7787). $C_{91}H_{122}N_4O_{35}$ (1830.8): calcd. C 59.66, H 6.71, N 3.06; found C 59.45, H 6.87, N 3.07.

**5-(Methoxycarbonyl)pentyl 3-*O*-Benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-2-*O*-methyl-α-D-mannopyranosyl-(1→2)-tetrakis[3-*O*-benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-α-D-mannopyranosyl]-3-*O*-benzyl-4-(2,4-di-*O*-acetyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-α-D-mannopyranoside (28):** Tetrasaccharide acceptor **26** (1.75 g, 0.96 mmol) was treated with donor 1**8** (1.15 g, 1.25 mmol) (Procedure B, Table 1) to give (1:1 hexane:acetone and 4:1→1:1 hexane/acetone, for analytical and preparative chromatography, respectively), a 5:1 mixture (NMR) of compounds **28** and **29**, which could be further resolved by chromatography (99:1→ 95:5 toluene/MeOH).

**Compound 28:** (1.60 mg, 62%), $[\alpha]_D$ = –10 (*c* = 1.1; $CHCl_3$). $^1$H NMR (600 MHz, $CDCl_3$): δ = 6.21–5.86 (m, 5 H, NH), 5.22–5.15 (m, 6 H, 6×2′-H), 5.04–4.98 (m, 4 H, H-$1^{II–V}$), 4.89 (br. s, 1 H, $1^{VI}$-H), 4.69 (br. s, 1 H, $1^{I}$-H), 4.66–4.43 (m, 12 H, 6C$H_2$Ph), 4.21–4.03 (m, 34 H, 6×4′a,b-H, $2^{II–V}$-H, $4^{I–VI}$-H), 3.87 (br. s, 1 H, $2^{I}$-H), 3.81–3.61 (m, 17 H, $2^{VI}$-H, $3^{I–VI}$-H, $5^{I–VI}$-H, 1a"-H, incl. 3.67, s, $COOCH_3$), 3.36, 3.35 (2t, *J* = 5.5 Hz, 1 H, 1b"-H), 3.24 (br. s, 3 H, $2^{VI}$-OMe), 2.32 (t, *J* = 7.1 Hz, 2 H, 5′′-H), 2.24–1.99 (m, 42 H, 6×3′a,b-H, incl. 9s, 2.17, 2.11, 2.06, 2.05, 2.04, 2.03, 2.02, 2.01, 2.00, 12$CH_3CO$), 1.69–1.53 (m, 4 H, 2′′-H, 4′′-H), 1.45–1.29 (m, 2 H, 3′′-H), 1.17–1.08 (m, 18 H, $6^{I–VI}$-H) ppm. $^{13}$C NMR (150 MHz, $CDCl_3$): δ = 174.53 ($COOCH_3$), 170.90, 170.82, 170.80 (6 C, 6NHCO), 169.73, 169.72, 169.71, 169.66, 169.60, 169.51, 169.36 (12 C, 12$CH_3CO$), 100.50 (2 C), 100.00, 99.79 (3 br. s, $J_{C,H}$ = 171.3, 169.0, 169.0 Hz, C-$1^{II–V}$), 99.06 (br. s, $J_{C,H}$ = 172.1 Hz, C-$1^{VI}$), 98.67 ($J_{C,H}$ = 170.4 Hz, C-$1^{I}$), 75.43, 75.31, 75.15, 74.80, 74.44, 74.06, 73.83, 73.69 (C-$2^{I,VI}$, C-$3^{I–VI}$), 73.25 (br. s, 4 C, C-$2^{II–V}$), 71.25, 71.20, 71.14, 71.12, 71.07, 71.05, 71.02, 71.00, 70.98, 70.68, 70.48, 70.44 (6×C-2′, 6$CH_2$Ph), 69.18, 69.00, 68.93, 68.89, 68.76, 67.59 (C-$5^{I–VI}$), 67.09 (C-1′′), 60.07, 59.99, 59.96, 59.93 (6 C, 6×C-4′), 59.03 ($OCH_3$-$2^{VI}$), 51.86, 51.80, 51.75, 51.63 (6 C, 6×C-$4^{I–VI}$), 51.58 ($COOCH_3$), 33.82 (C-5′′), 30.95, 30.94, 30.87 (6 C, 6×C-3′), 28.56 (C-2′′), 25.62 (C-3′′), 24.26 (C-4′′), 20.84, 20.83, 20.75, 20.73, 20.67 (12 C, 12$CH_3CO$), 18.80, 18.05, 18.03 (6 C, C-$6^{I–VI}$) ppm. ESI-MS: *m*/*z*: 2732.5002 ([M –1 + 2 Na]$^+$; calcd. 2732.1237). $C_{134}H_{178}N_6O_{51}$ (2688.9): calcd. C 59.86, H 6.67, N 3.13; found C 59.73, H 6.76, N 3.13.

**Compound 29:** (350 mg, 13%). $^1$H NMR (600 MHz, $CDCl_3$): δ = 6.40–5.92 (m, 4 H, NH), 5.30–5.11 (m, 7 H, 6×2′-H, incl. 5.27, br. s, $1^{VI}$-H), 5.11, 5.02, 5.00 (3s, 3 H, H-$1^{II–IV}$), 4.82–4.38 (m, 1-H$^{I}$, $J_{1,2}$ = 1.4 Hz, 12 H, 11C*H*Ph, incl. 4.75, d), 4.37–3.93 (m, 24 H, C*H*Ph, 6×4′a,b-H, $4^{I–VI}$-H, $2^{I–IV}$-H, $5^{V}$-H, incl. s, 4.29, $1^{V}$-H), 3.86–3.65 (m, 17 H, $2^{V,VI}$-H, $3^{I–VI}$-H, $5^{I–IV,VI}$-H, 1a"-H, incl. 3.67, s, $OCH_3$), 3.40, 3.38 (2t, *J* = 5.5 Hz, 1 H, 1b"-H), 3.26 (br. s, 3 H, $2^{VI}$-OMe), 2.34 (t, *J* = 7.1 Hz, 2 H, 5′′-H), 2.24–1.83 (m, 42 H, 6×3′a,b-H, incl. 11s, 2.15, 2.08, 2.05, 2.03, 2.01, 2.00, 1.99, 1.98, 1.97, 1.96, 1.95, 12$CH_3CO$), 1.66–1.53 (m, 4 H, 2′′-H, 4′′-H), 1.47–1.26 (m, 2 H, 3′′-H), 1.23–1.08 (m, 18 H, $6^{I–VI}$-H) ppm. $^{13}$C NMR (150 MHz, $CDCl_3$): δ = 174.50 ($COOCH_3$), 170.80, 170.69, 170.68, 170.67, 170.62, 170.59 (6NHCO), 169.93, 169.77, 169.69, 169.62, 169.61, 169.51, 169.34, 169.18 (12 C, 12$CH_3CO$), 100.54, 100.15, 99.65 (3br. s, C-$1^{II–IV}$), 98.88 ($J_{C,H}$ = 172.0 Hz, C-$1^{I}$), 97.65 ($J_{C,H}$ = 175.0 Hz, C-$1^{VI}$), 97.53 ($J_{C,H}$ = 155.0 Hz, C-$1^{V}$), 75.59, 76.79, 76.67, 76.33, 75.47, 74.25, 73.77, 73.10, 72.54 (12 C, C-$2^{I–VI}$, C-$3^{I–VI}$), 71.59, 71.33, 71.21, 71.11, 71.04, 70.95, 70.86, 70.65 (12 C, 6×C-2′, 6$CH_2$Ph), 69.58, 69.07, 68.93, 68.85, 67.99, 67.63 (C-$5^{I–VI}$), 66.89 (C-1′′), 60.48, 60.09, 59.89, 59.86, 59.77 (6 C, 6×C-4′), 59.34 ($OCH_3$-$2^{VI}$), 53.37, 52.42, 52.18, 51.94, 51.70, 51.54 (6×C-$4^{I–VI}$), 51.49 ($COOCH_3$), 33.73 (C-5′′), 30.94, 30.87, 30.83, 30.78, 30.69, 30.54 (6×C-3′), 28.41 (C-2′′), 25.48 (C-3′′), 24.11 (C-4′′), 20.77, 20.74, 20.67, 20.65, 20.63, 20.58, 20.54, 20.50 (12 C, 12$CH_3CO$), 18.20, 18.05, 17.94, 17.87, 17.57 (6 C, C-$6^{I–VI}$) ppm.

**5-(Methoxycarbonyl)pentyl 3-*O*-Benzyl-4-(3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-2-*O*-methyl-α-D-mannopyranosyl-(1→2)-tetrakis[3-*O*-benzyl-4-(3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-α-D-mannopyranosyl]-3-*O*-benzyl-4-(3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-α-D-mannopyranoside (31):** 0.1 M NaOMe was added to a solution of the hexasaccharide **28** (1.1 g, 0.41 mmol) in MeOH (200 mL) until the pH was strongly alkaline to litmus. The mixture was kept overnight at room temperature, when TLC (4:1:0.1 $CH_2Cl_2$/MeOH-AcOH) showed that the reaction was complete. After neutralization (Amberlite IR-120, $H^+$-resin), chromatography (85:15 $CH_2Cl_2$/MeOH), gave the deacetylated compound **30** (705 mg, 80%). $^1$H NMR (300 MHz, $CD_3OD$): δ = 5.11–5.03 (4d, $J_{1,2}$ = 1.5, 1.5, 1.5, 2.1 Hz, 4 H, H-$1^{II–V}$), 4.87 (d, $J_{1,2}$ = 1.8 Hz, 1 H, $1^{VI}$-H), 4.77 (d, $J_{1,2}$ = 1.4 Hz, 1 H, $1^{I}$-H), 4.54–4.68 (m, 12 H, 6C$H_2$Ph), 4.24–4.04 (m, 24 H, 6×2′-H, $2^{II–V}$-H, $4^{I–VI}$-H), 4.02–3.64 (m, 30 H, 1a"-H, $2^{I,VI}$-H, $3^{I–VI}$-H, 6×4′a,b-H, $5^{I–VI}$-H, incl. 3.65, s, $COOCH_3$), 3.40, 3.38 (2t, *J* = 5.5 Hz, 1 H, 1b"-H), 3.15 (br. s, 3 H, $2^{VI}$-OMe), 2.33 (t, *J* = 7.2 Hz, 2 H, 5′′-H), 2.10–1.95 (m, 6 H, 6×3′a-H), 1.82–1.52 (m, 10 H, 6×3′b-H, 4′′-H, 2′′-H, in that order), 1.45–1.36 (m, 2 H, 3′′-H), 1.20–1.01 (m, 18 H, $6^{I–VI}$-H) ppm. $^{13}$C NMR (75 MHz, $CD_3OD$): δ = 177.88, 177.83, 177.80, 177.63 (6 C, 6×NHCO), 176.05 ($COOCH_3$), 102.42, 102.27, 102.19 (4 C, C-$1^{II–V}$), 100.47 (C-$1^{VI}$), 100.40 (C-$1^{I}$), 77.51, 77.11, 76.88, 76.20, 76.06, 75.82, 75.80 (12 C, C-$2^{I–VI}$, C-$3^{I–VI}$), 73.25, 72.98, 72.88, 72.81, 72.50 (6×$CH_2$Ph), 70.88 (6 C, 6×C-2′), 70.05, 70.04, 70.03, 69.87, 69.31 (6 C, C-$5^{I–VI}$), 68.60 (C-1′′), 59.94 (6 C, 6×C-4′), 59.10 ($OCH_3$-$2^{VI}$), 53.49, 53.29, 53.01 (6 C, 6×C-$4^{I–VI}$), 52.26 ($COOCH_3$), 33.60 (C-5′′), 34.78 (6 C, 6×C-3′), 30.11 (C-2′′), 26.91 (C-3′′), 25.74 (C-4′′), 18.74, 18.63, 18.60, 18.50 (6 C, C-$6^{I–VI}$) ppm. ESI-MS: *m*/*z*: 2230.0064 ([M + 1 + 2 Na]$^{3+}$; calcd. 2230.0125); 2229.0034 ([M + 2 Na]$^{2+}$; calcd. 2229.0047).

A mixture of the foregoing compound **30** (640 mg, 0.29 mmol) and 5% Pd-C (600 mg) in MeOH (50 mL) was stirred under hydrogen pressure (100 psi) for 4 h, when TLC (1:1:0.1 $CHCl_3$/MeOH-AcOH) showed that the debenzylation was complete and that one product was formed. After filtration through a celite pad, the filtrate was concentrated chromatographed (3:2:0.1 $CHCl_3$/MeOH/AcOH) and a solution of the product was freeze-dried to give pure **31** (430 mg, 90%) as a white amorphous solid, which was identical with the previously, independently synthesized substance.[18] $^1$H NMR (600 MHz, $D_2O$): δ = 5.21 (d, $J_{1,2}$ = 1.8 Hz, 1 H, $1^{VI}$-H), 5.19, 5.17, 5.16, 5.15 (4d, $J_{1,2}$ = 1.6, 1.5, 1.5, 1.3 Hz, 4 H, H-$1^{II–V}$), 4.89 (d, $J_{1,2}$ = 1.6 Hz, 1 H, $1^{I}$-H), 4.31–4.27 (m, 6 H, 6×2′-H), 4.19–3.86 (m, $4^{I}$-H, $J_{2,3}$ = 3.3, $J_{3,4}$ = 10.6 Hz, $3^{VI}$-H; dd, 4.05, $J_{2,3}$ = 3.2, $J_{3,4}$ = 10.3 Hz, $3^{I}$-H; t, 3.92, *J* = 10.3 Hz, 18 H, $2^{I–V}$-H, $3^{II–V}$-H, $5^{I–VI}$-H, incl. dd, 4.07), 3.83 (t, *J* = 10.4 Hz, $4^{VI}$-H), 3.77 (dd, 1 H, $2^{VI}$-H), 3.78–3.76 (m, 12 H, 6×4′a,b-H), 3.72, 3.70 (2t, *J* = 6.1 Hz, 1 H, 1a"-H), 3.68 (s, 3 H, $COOCH_3$), 3.55, 3.53 (2t, *J* =

6.1 Hz, 1 H, 1b"-H), 3.49 (s, 3 H, $2^{VI}$-OMe), 2.40 (t, $J$ = 7.4 Hz, 2 H, 5′′-H), 2.07–2.00 (m, 6 H, 6×3′a-H), 1.88–1.81 (m, 6 H, 6×3′b-H), 1.65–1.59 (m, 4 H, 4′′-H, 2′′-H), 1.42–1.39 (m, 2 H, 3′′-H), 1.20–1.17 (m, 15 H, $6^{I–V}$-H), 1.14 (d, $J_{5,6}$ = 6.2 Hz, 3 H, $6^{VI}$-H) ppm. $^{13}$C NMR (150 MHz, $D_2O$): $\delta$ = 183.42 ($C$OOCH$_3$), 180.32, 180.18, 180.17, 180.16, 180.01 (6 C, 6NHCO), 103.57, 103.48, 103.46, 103.42 (C-$1^{II–V}$), 100.67 (C-$1^{VI}$), 100.14 (C-$1^{I}$), 81.65 (C-$2^{VI}$), 80.47 (C-$2^{I}$), 80.27, 79.97, 79.94, 79.88 (C-$2^{II–V}$), 71.70 (6 C, 6×C-2′), 71.01, 70.99, 70.73, 70.56, 70.41, 70.32, 70.21, 70.17, 70.13 (12 C, C-$3^{I–VI}$, C-$5^{I–VI}$), 70.64 (C-1′′), 61.48 (OCH$_3$-$2^{VI}$), 60.57 (6 C, 6×C-4′), 55.87, 55.81, 55.69, 55.64 (6 C, 6×C-$4^{I–VI}$), 54.86 (COO$C$H$_3$), 38.72, 38.70, 38.66 (6 C, 6×C-3′), 36.33 (C-5′′), 30.80 (C-2′′), 27.59 (C-3′′), 26.72 (C-4′′), 19.63, 19.59, 19.58, 19.53, 19.52 (6 C, C-$6^{I–VI}$) ppm. ESI-MS: $m/z$: 1665.7369 ([M + Na]$^+$; calcd. 1665.7426).

## Acknowledgments

This research was supported by the Intramural Research Program of the National Institutes of Health (NIH), National Institute of Diabetes and Digestive and Kidney (NIDDK).

[1] S. Chatterjee, K. Chaudhuri, *Biochim. Biophys. Acta* **2003**, *1639*, 65–79.
[2] N. W. Preston, *Lancet* **1993**, *342*, 925–926.
[3] M. P. Aanning, U. H Stroeher, R. Morona, in: *Vibrio cholerae and Cholera: Molecular to Global Perspectives* (I. K. Wachsmuth, P. A. Blake, O. Olsvik), American Society for Microbiology: Washington, D. C., **1994**, p. 77–94.
[4] K. Hisatsune, S. Kondo, Y. Isshiki, T. Iguchi, Y. Haishima, *Biochem. Biophys. Res. Commun.* **1993**, *190*, 302–307.
[5] K. Hisatsune, S. Kondo, Y. Isshiki, T. Iguchi, Y. Haishima, *Biochem. Biophys. Res. Commun.* **1993**, *194*, 584.
[6] T. Ito, T. Higuchi, M. Hirobe, K. Hiramatsu, T. Yokota, *Carbohydr. Res.* **1994**, *256*, 113–128.
[7] T. Peters, D. R. Bundle, *Can. J. Chem.* **1989**, *67*, 497–502.
[8] D. R. Bundle, M. Gerken, T. Peters, *Carbohydr. Res.* **1988**, *174*, 239–251.
[9] Y. Ogawa, P.-s. Lei, P. Kováč, *Bioorg. Med. Chem. Lett.* **1995**, *5*, 2283–2286.
[10] M. Gotoh, P. Kováč, *J. Carbohydr. Chem.* **1994**, *13*, 1193–1213.
[11] P.-s. Lei, Y. Ogawa, P. Kováč, *Carbohydr. Res.* **1996**, *281*, 47–60.
[12] R. Adamo, P. Kováč, *Eur. J. Org. Chem.* **2006**, 2803–2809.
[13] A. Arencibia-Mohar, A. Ariosa-Alvarez, O. Madrazo-Alonso, E. G. Abreu, L. Garcia-Imia, G. Sierra-Gonzalez, V. Verez-Bencomo, *Carbohydr. Res.* **1998**, *306*, 163–170.
[14] J. H. van Boom, P. M. J. Burgers, *Tetrahedron Lett.* **1976**, *17*, 4875–4878.
[15] T. Zhu, G.-J. Boons, *Chem. Eur. J.* **2001**, *7*, 2382–2389.
[16] R. Saksena, X. Ma, P. Kováč, T. K. Wade, *Carbohydr. Res.* **2005**, *340*, 2256–2269.
[17] A. Chernyak, S. Kondo, T. K. Wade, M. D. Meeks, P. M. Alzari, J.-M. Fournier, R. K. Taylor, P. Kováč, W. F. Wade, *J. Infect. Dis.* **2002**, *185*, 950–962.
[18] Y. Ogawa, P.-s. Lei, P. Kováč, *Carbohydr. Res.* **1996**, *293*, 173–194.
[19] J. Zhang, P. Kováč, *Carbohydr. Res.* **1997**, *300*, 329–339.
[20] X. Ma, R. Saksena, A. Chernyak, P. Kováv, *Org. Biomol. Chem.* **2003**, *1*, 775–784.
[21] Y. Ogawa, P. Kováč, *Glycoconjugate J.* **1997**, *14*, 433–438.
[22] R. Saksena, J. Zhang, P. Kováč, *Tetrahedron: Asymmetry* **2005**, *16*, 187–197.
[23] P. Kováč, L. Lerner, *Carbohydr. Res.* **1988**, *184*, 87–112.
[24] J. Kihlberg, E. Eichler, D. R. Bundle, *Carbohydr. Res.* **1991**, *211*, 59–75.
[25] H. R. Geurtsen, G.-J. Boons, *Tetrahedron Lett.* **2002**, *43*, 9429–9431.
[26] D. A. Leigh, J. P. Smart, A. M. Truscallo, *Carbohydr. Res.* **1995**, *276*, 417–424.
[27] H. Tanaka, M. Adachi, T. Takahashi, *Tetrahedron Lett.* **2004**, *45*, 1433–1436.
[28] T. Adachi, Y. Yamada, I. Inoue, M. Saneyoshi, *Synthesis* **1977**, 45–46.
[29] P. Fugedi, P. Nanasi, *J. Carbohydr. Nucleo. Nucleot.* **1981**, *8*, 547–555.
[30] P. Kováč, in: *Handbook of Derivatives for Chromatography*, 2 ed. (Eds.: K. Blau, J. M. Halket), John Wiley & Sons, Chichester, **1993**, p. 109–129.
[31] A. Demchenko, T. Stauch, G.-J. Boons, *Synlett* **1997**, 818–819.
[32] R. Saksena, X. Ma, P. Kováč, *Carbohydr. Res.* **2003**, *338*, 2591–2603.
[33] T. Peters, D. R. Bundle, *Can. J. Chem.* **1989**, *67*, 491–496.
[34] J. C. Gast, R. H. Atalla, R. D. McKelvey, *Carbohydr. Res.* **1980**, *84*, 137–146.
[35] P. Kováč, J. Hirsch, *Carbohydr. Res.* **1982**, *100*, 177–193.
[36] G. Solladie, C. Ziani-Cherif, *J. Org. Chem.* **1993**, *58*, 2181–2185.

Received: September 28, 2006
Published Online: December 21, 2006