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4′-Methoxyphenacyl-Assisted Synthesis of β-Kdo Glycosides

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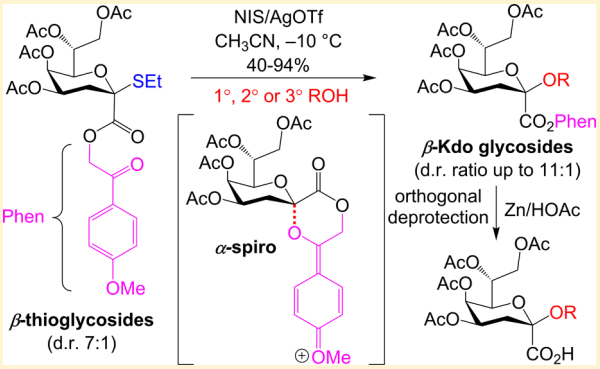
Supporting Information

ABSTRACT: 3-Deoxy-β-D-*manno*-oct-2-ulosonic acid (β-Kdo) glycosides are mainly found in capsular polysaccharides and extracellular exopolysaccharides from Gram-negative bacteria. These compounds have profound biological implications in immune response and act as virulence factors. We have developed a novel methodology for the stereoselective synthesis of β-Kdo glycosides via the use of a 4′-methoxyphenacyl (Phen) auxiliary group at the C1 position of a peracetylated β-Kdo thioglycoside. Under the promotion of NIS/AgOTf in acetonitrile, a series of Kdo glycosides was synthesized in good yield and β-selectivity while minimizing the formation of undesirable glycals. Stereoselectivity of the glycosylation was shown to be modulated by various factors such as promotor, solvent, anomeric ratio of donor, nature of acceptor, and Phen substitution. Chemoselective cleavage of the Phen group was performed under the action of Zn/HOAc. DFT calculations together with experimental results suggested that α-triflate and a six-membered α-spiroPhen are plausible intermediates of the reaction, accounting for the enhanced formation of β-Kdo glycosides. The developed methodology could be applied to the synthesis of β-Kdo-containing glycans from pathogenic bacteria.



INTRODUCTION

3-Deoxy-D-*manno*-oct-2-ulosonic acid (Kdo) glycosides are mainly found in the surface polysaccharides of bacteria.[1] Kdo glycosides with the α-configuration are present in virtually all of the lipopolysaccharide (LPS) core regions of Gram-negative bacteria, playing a crucial role in the structural integrity of bacterial membranes.[2] In contrast, β-Kdo glycosides occur far less frequently within LPS. Rare occurrences include (1) LPS core regions from *Alteromonas macleodii*,[3] (2) LPS O-antigen (OAg) from *Providencia alcalifaciens*,[4] and (3) the nonreducing end of LPS OAg from *Klebsiella pneumoniae* serotype O12.[5] The most frequent occurrence of β-Kdo glycosides is within the repeating unit of capsular polysaccharides (CPS),[1] which are known as virulence factors and are involved in protection from host immune mechanisms.[6] For instance, *Kingella kingae*, a Gram-negative bacteria causing septic arthritis, osteomyelitis, and bacteremia in young children, produces a CPS featuring a repeating disaccharide comprised of a Kdo residue in the β-configuration (Figure 1).[7] β-Kdo glycosides have also been found in extracellular exopolysaccharides (EPS), such as the one expressed by the "Tier 1 Select Agent" *Burkholderia pseudomallei*, the causative agent of melioidosis.[8−10] Cytidine monophosphate

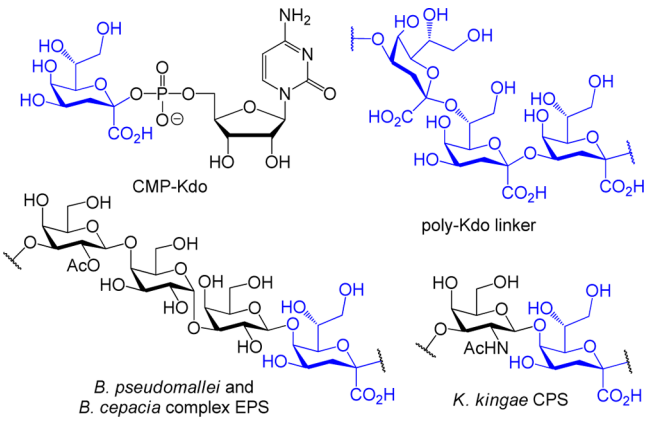


Figure 1. Naturally occurring β-Kdo-containing glycans from bacteria.

(CMP)-Kdo,[11,12] the activated sugar nucleotide processed by Kdo glycosyltransferases, is another important example of a

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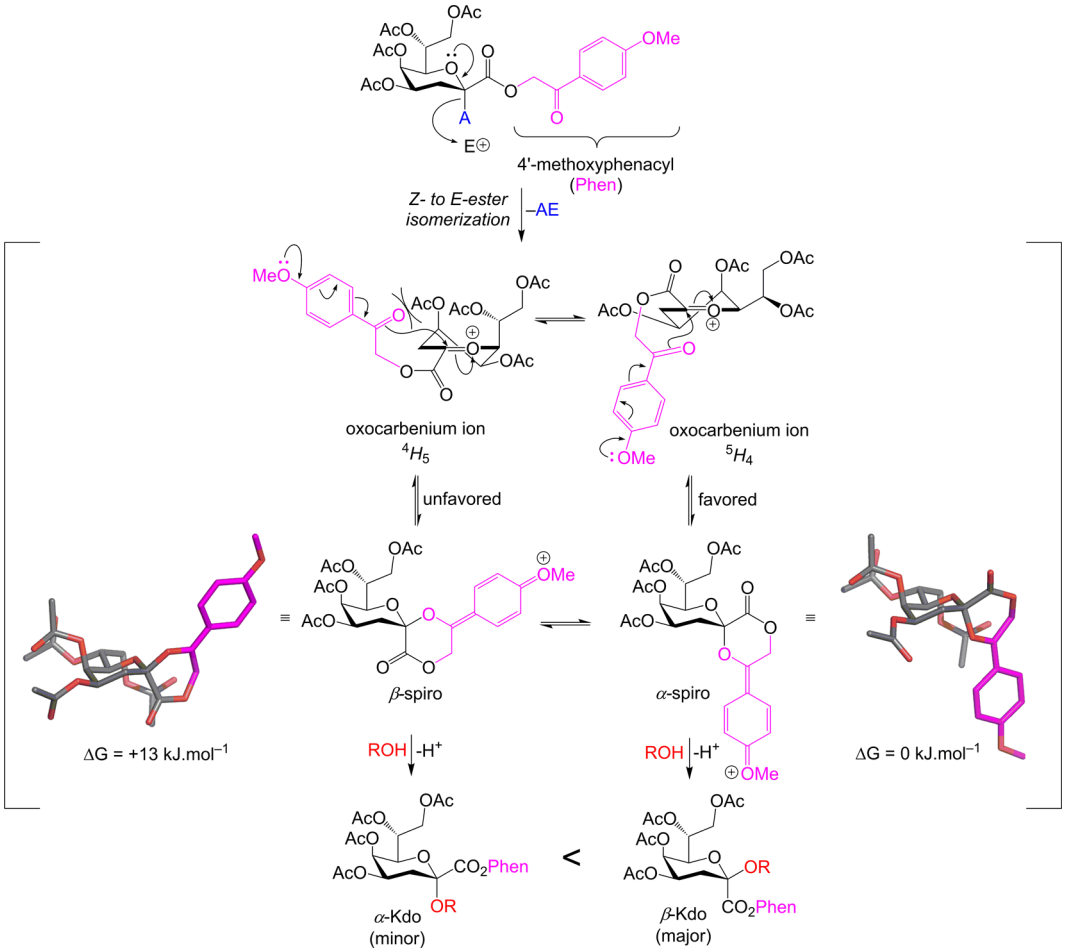

Figure 2. Proposed approach for the synthesis of β-Kdo glycosides through the use of a 4′-methoxyphenacyl (Phen) C1-auxiliary group. A = activating group; E = electrophile. The 3D structures were obtained by DFT geometrical optimization at the B3LYP/6-311++G(2d,2p) level of theory (hydrogen atoms have been omitted for the sake of clarity).

naturally occurring compound bearing a β-Kdo unit. Recently, Whitfield and co-workers[13] have highlighted the presence of poly-Kdo linkers containing alternating β-(2 → 4) and β-(2 → 7) linkages at the reducing end of CPS from various Gram-negative pathogens including *Escherichia coli*, *Campylobacter jejuni*, *Haemophilus influenza*, *Neisseria meningitides*, and *Pasteurella multocida*. Enzymes involved in the biosynthesis of these poly-Kdo linkers have been characterized as novel retaining Kdo transferases (KpsC and KpsS).[14,15] Owing to the structural significance and biological importance of β-Kdo residues in bacterial polysaccharides, straightforward synthetic routes toward β-Kdo glycosides are needed.[16,17] Access to these compounds in pure and homogeneous forms would further the development of vaccines, diagnostics, and therapeutics against some clinically relevant bacterial pathogens.[1,2,18]

The synthesis of Kdo glycosides is not a trivial task and shares similarities with the glycosylation of *N*-acetylneuraminic acid (Neu5Ac).[19] The lack of a hydroxyl group at the C3 position, which hampers the use of the neighboring group participation effect, the presence of an electron-withdrawing carboxylic acid at C1, which deactivates and hinders the anomeric position, and the undesirable formation of 2,3-glycals are the main issues regarding the synthesis of Kdo glycosides.[16,17] In the past few years, novel methodologies have been implemented to allow access to α-Kdo glycosides in excellent yields and stereoselectivity. In this respect, it is worth mentioning the use of 5,7-*O*-di-*tert*-butylsilylene-protected thioglycoside[20] and 3-iodo fluoride[21−23] donors. However, the synthetic chemistry of Kdo glycosides having the opposite thermodynamically less stable β-configuration (OR group in equatorial rather than axial position) still requires improvement.[16]

Toward this aim, Ling and co-workers,[24] relying on the pioneering work of Takahashi,[25] developed a novel class of 4,5;7,8-di-*O*-isopropylidene-protected 1-*C*-arylglycal donors, which upon treatment with *N*-iodosuccinimide (NIS), led to the stereoselective formation of β-Kdo glycosides. However, their approach required a supplemental reductive deiodination step followed by an oxidative transformation in order to provide the carboxylic acid at C1. Recently, Mong and co-workers[26] partially resolved the latter issue by preparing Kdo glycal donors bearing a preinstalled carboxylate at C1. NIS-mediated glycosylation of these glycals in a DCM/CH_3CN mixture led to β-Kdo glycosides in a β/α ratio of up to 20:1 following radical deiodination. In both previous cases, the presence of a 4,5-*O*-isopropylidene group locking the pyranose ring into a skew-boat conformation was found to be essential for providing high β-stereoselectivity. Using unlocked perbenzylated or peracetylated Kdo glycals led to the opposite *trans*-diaxial selectivity with regard to the C3 iodine atom and C2 OR group.[25,27]

There have been few reports regarding the synthesis of β-Kdo glycosides with "nonglycal" donors. van Boom and co-workers[28,29] were the first to show that reacting peracetylated β-Kdo

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thioglycosides with NIS/TfOH could provide Kdo glycosides in the major β-configuration when 3-amino-*N*-[(benzyloxy)-carbonyl]-1-propanol was used as an acceptor. More recently, an interesting study by the group of Oscarson[27] revealed that peracylated β-Kdo thioglycosides were suitable donors for the formation of β-Kdo glycosides bearing 2-[4-(trifluoroacetamido)phenyl]ethyl as a spacer when DMTST or IBr/AgOTf was used as the promoter. In all these studies, however, no systematic evaluations of the glycosylation conditions were performed, and no mechanistic details were provided. Herein, we report a novel approach for the stereoselective synthesis of β-Kdo glycosides involving the use of a long-range participating 4′-methoxyphenacyl (Phen) auxiliary group at the C1 position. Glycosylation conditions were thoroughly investigated both in the presence and in the absence of the Phen group, e.g., promoters, leaving groups, anomeric configuration of donors, solvents, nature of acceptors, addition order of reagents, and counteranions. On the basis of DFT calculations and experimental details, we also propose plausible intermediates accounting for the formation of both α- and β-Kdo glycosides under the optimized reaction conditions.

■ RESULTS AND DISCUSSION

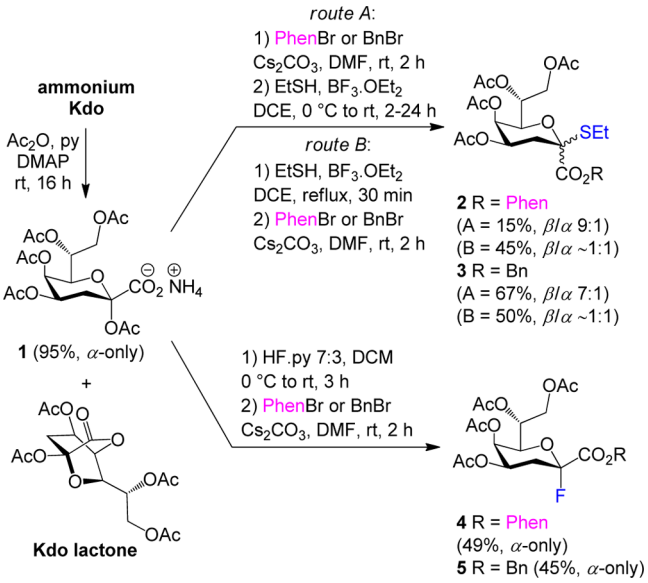
Synthetic Approach. Long-range participating effects through the use of an auxiliary group have been previously described for the synthesis of α-Neu5Ac glycosides, which display structural similarities with β-Kdo glycosides. The presence of ester chains at the C1 position of Neu5Ac, such as 2-(methylthio)ethyl, 2-(phenylthio)ethyl,[30] and *N*,*N*-dimethylglycolamide,[31,32] was shown to enhance the α-selectivity of the glycosylation reaction via the stabilization of the oxocarbenium ion from the β-axial orientation, thereby favoring the attack of the nucleophile from the α-face. Enhanced α-selectivities were also observed for Neu5Ac thioesters[33] and 2-cyanoethyl esters[34] in conjunction with CH_3CN, presumably through a mechanism involving stabilization of the β-oriented nitrilium ion.

Inspired by these previous studies, we have devised an analogous approach to tackle the problem of β-Kdo glycosides synthesis via the use of a 4′-methoxyphenacyl (Phen) auxiliary group at the C1 position of peracetylated Kdo donors. Our choice was driven by two important factors: (1) the enhanced electronic density of the ketone functionality that would be likely to participate favorably in the course of the glycosylation reaction, and (2) the orthogonality of phenacyl groups[35] with several base- and acid-sensitive protecting groups that would be an asset over previously reported auxiliary groups.

Our working hypothesis is depicted in Figure 2. Once the Kdo donor is activated by a suitable electrophilic promoter, the oxocarbenium ion (glycosyl cation)[36] will be formed. According to Woerpel,[37−40] the attack of the electron-rich ketone from the α-face of the $^5H_4$ half-chair conformer would be favored in order to minimize the destabilizing 1,3-diaxial interactions. The resulting six-membered α-spiro compound, which could be found either as a covalent or contact ion pair intermediate, would then be attacked by the acceptor preferentially from the opposite β-face, leading to enhanced β-selectivity for the formation of Kdo glycosides. DFT calculations at the B3LYP/6-311++G(2d,2p) level of theory tend to support this hypothesis since the α-spiro intermediate was found to be energetically favored compared to the β-spiro intermediate by 13.0 kJ·mol^{-1} (see Figure S1 and Table S1). Moreover, these two intermediates were at least 36.8 kJ·mol^{-1} more stable than the free oxocarbenium ion. Nevertheless, it is important to point out that, in the case of a Curtin−Hammett scenario in which there is a rapid exchange between both intermediates, the major product could also arise from the higher energy ground-state intermediate.[41,42] Furthermore, it has to be stressed that a conformational change from the more stable *Z*-ester to the less stable *E*-ester must occur in order to allow the phenacyl ketone to approach the glycosyl cation. According to the literature, the energy difference for the *Z*/*E* ester isomerization is about 12.5 kJ·mol^{-1}.[43] This energy barrier can be lowered by using polar solvents, such as acetonitrile, or when an electron-withdrawing group is attached to the R′ position of a RCO_2R' ester, such as a phenacyl group.[44] In the case of our work, the *Z*/*E* ester isomerization would be beneficial in terms of energy because it opens the way for the formation of the spiro intermediates, which are more stable than the free oxocarbenium ion.

Synthesis of Kdo Donors. The synthesis of peracetylated Kdo thioglycoside and fluoride donors **2**−**5** bearing participating (Phen) or nonparticipating (Bn) ester groups was investigated first (Scheme 1). Crystalline ammonium Kdo was obtained through the modified Cornforth procedure[45−47] using an optimized methodology recently reported by Kosma.[48] This allowed us to prepare gram quantities of pure Kdo in a reliable manner. Ammonium Kdo was subjected to acetylation under standard conditions (Ac_2O, py, DMAP, rt) leading to peracetylated **1**[49] with nearly quantitative yield. Performing the reaction at more elevated temperatures (>30 °C) generated substantial amounts of Kdo lactone.[50] Then, two different routes were studied for the synthesis of thioglycosides **2** and **3**. Esterification with 4′-methoxyphenacyl bromide (PhenBr) or BnBr in the presence of Cs_2CO_3 followed by glycosylation with EtSH under the action of $BF_3{\cdot}OEt_2$ produced donors **2** and **3** in 15 and 67% yield, respectively, both predominantly featuring the β-configuration as expected[27] (β/α 9:1 for **2** and 7:1 for **3**). The low yield obtained for the Phen derivative **2** was due to the formation of an undesirable byproduct, presumably a dithioketal arising from the addition of two EtSH molecules on the activated ketone (LRMS: m/z $[M + Na]^+$ calcd for $C_{31}H_{44}O_{12}S_3$ 727.2, found 727.7). Another route was then investigated in which free

Scheme 1. Synthesis of Kdo Thioglycoside and Fluoride Donors



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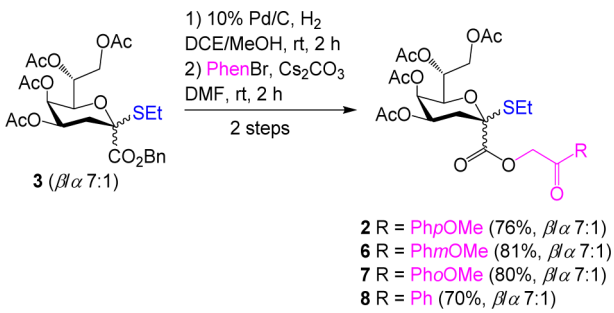
acid **1** was first refluxed in DCE with EtSH and $BF_3{\cdot}OEt_2$ followed by esterification of the resulting thioglycoside. Using this route, donors **2** and **3** were obtained in convenient yields (45 and 50%, respectively) but with anomeric ratios different from those of route A ($\beta/\alpha \sim 1{:}1$). Fluoride donors **4** and **5** were synthesized via a similar approach. Regioselective fluorination at the anomeric position was performed by treatment of peracetylated **1** with HF·py 7:3 followed by standard esterification to provide donors **4** and **5** with 49 and 45% yield, respectively.[51] The exclusive α-configuration of these fluoride donors was confirmed by ^{19}F NMR analysis ($^3J_{F,H3ax}$ = 34.6 Hz, $^3J_{F,H3eq}$ = 6.0 Hz).

In order to provide donor **2** with the same anomeric ratio as **3** (β/α 7:1, route A) and to improve the yield, an additional methodology was investigated for comparison purposes (Scheme 2). Therefore, hydrogenolysis of thioglycoside **3**

Scheme 2. Synthesis of β-Kdo Thioglycoside Bearing Diversely Substituted Phenacyl Groups



followed by esterification under the above-mentioned conditions provided donor **2** with good yield (76%) without erosion of diastereoselectivity (β/α 7:1). Furthermore, this approach allowed us to synthesize Kdo thioglycoside donors bearing 3′-methoxy (**6**) and 2′-methoxy (**7**) as well as unsubstituted (**8**) phenacyl groups, all having the same β/α ratio (7:1).

Synthesis of β-Kdo Glycosides. With Kdo donors **2**−**8** in hand, study of their glycosylation behavior for the selective formation of β-Kdo glycosides was investigated next. Using Phen thioglycoside **2** in a ∼ 1:1 β/α ratio together with 5-amino-*N*-benzyloxycarbonyl-1-pentanol (**9**,[52] Figure 3) as a model

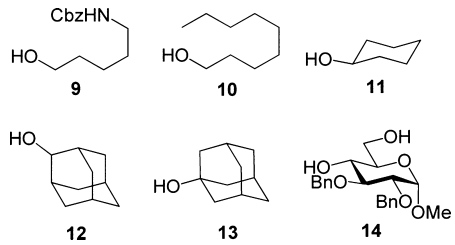


Figure 3. Glycosyl acceptors (**9**−**14**) used in this study.

acceptor, we first screened different thiophilic promoters (Table 1). Glycosylation reactions in entries 1−8 were conducted in the nonparticipating solvent DCE at −10 °C in the presence of water-scavenging 4 Å molecular sieves, and the β/α selectivity ratio was evaluated by ^{1}H NMR analysis. At this temperature, all promoters were shown to give excellent conversions (>95%), with the exception of MeOTf (60%), while β-anomeric selectivity varied significantly.

In contrast with the results of Oscarson,[27] the use of IBr/AgOTf[53] gave the lowest β/α ratio (1.5:1.0) without formation of glycal **16** (entry 1). We interpreted this result as a competitive attack of the nucleophilic bromide anion at the anomeric center, forming a reactive β-bromide species[54] that can be displaced from the α-face by the acceptor. Using Me_2S_2/MeOTf (DMTST)[55] or Me_2S_2/Tf_2O[56] provided better β-selectivity (up to 3.7:1.0), but glycal formation was observed (entries 3 and 4). Enhanced formation of Kdo glycoside **15*β*** was observed with *N*-chlorosuccinimide (NCS)/TfOH as the promoter (β/α 5.0:1.0), but again, substantial amounts of glycal **16** were formed (entry 5). Switching to NIS[57−59] significantly decreased the formation of **16** but kept good β-selectivity (entry 6). Conducting the reaction at −40 °C with NIS/TfOH prevented glycal formation (entry 7); however, consumption of the donor was not complete (∼41%).

We next examined the use of NIS/AgOTf[59] as the promoter, which gave the best results in terms of β-selectivity while minimizing glycal formation (entry 8). This result was somewhat unexpected since Oscarson[27] showed that a similar peracetylated methyl ester Kdo thioglycoside only furnished elimination product following treatment by NIS/AgOTf in DCM. We then explored the use of well-known participating solvents such as Et_2O and CH_3CN (entries 9 and 10).[60] The outcome of these reactions was found to be promising: complete conversion of donor **2**, enhanced β-selectivity, and no formation of glycal were observed. The reaction in CH_3CN was performed on a 1.25 mmol scale to provide Kdo glycoside **15** in 84% yield with a β/α ratio of 7.9:1.0. We hypothesized that preactivation conditions[61] would be valuable in order to favor the formation of the α-spiro intermediate and would thereby potentially enhance the β-selectivity. Unfortunately, premixing donor **2** with NIS/AgOTf before adding acceptor **9** led exclusively to glycal **16** in both participating (CH_3CN) and nonparticipating (DCE) solvents (entries 11 and 12). The effect of counteranions[62,63] was also studied. Therefore, promoters containing anions less coordinating than OTf^- such as NIS/$AgClO_4$ and NIS/$AgBF_4$ were evaluated (entries 13 and 14). Using these promoters, β-selectivity decreased by more than 2-fold, implying that the reaction intermediates were sensitive to the strength of the coordinating anion. On the basis of this result, we can hypothesize that a covalently bound (or contact ion pair) triflate could be one of the intermediates involved in the glycosylation reaction, although this has not been experimentally proven.

These results were then compared to those obtained with donor **3** (β/α ratio of ∼1:1) bearing a nonparticipating benzyl ester at C1 (Table 2). The advantage of using the Phen auxiliary group was clearly demonstrated here. Indeed, under the promotion of NIS/AgOTf, enhanced β-selectivity was obtained with donor **2** compared to donor **3** (entries 1 to 4). Notably, the β/α ratio increased by more than 2-fold when CH_3CN was used as the solvent (7.9:1.0). Impact of the starting anomeric ratio of donors **2** and **3** was investigated next (entries 5−10). As shown in previous studies,[28,29] performing the reaction with Kdo thioglycosides as major β-anomer (7.0:1.0) significantly improved β-selectivity (up to β/α 11.0:1.0 in CH_3CN, entry 8). For all of these reactions, donor **2** bearing a Phen group provided better β-selectivity than benzyl ester **3** and no glycal (**16** or **18**) was detected. As previously mentioned, the use of IBr instead of NIS decreased selectivity. Next, reactions were performed with α-fluoride donors **4** and **5** in order to probe the impact of the leaving group (entries 11 and 12). $BF_3{\cdot}OEt_2$ (6 equiv) was needed to ensure full conversion of these fluorides.[64]

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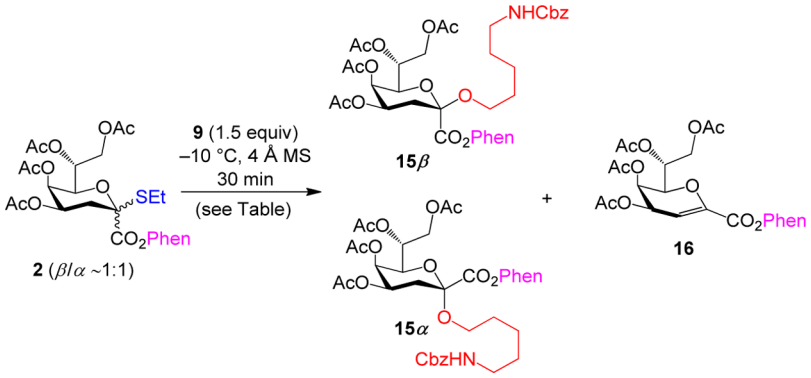
Table 1. Synthesis of β-Kdo Glycosides: Promoter and Solvent Screening



entry	promoter	solvent	conv[a] (%)	selectivity ratio[a] 15β	15α	16
1	IBr/AgOTf	DCE	>95	1.5	1.0	nd[b]
2	MeOTf	DCE	60	2.4	1.0	0.8
3	Me_2S_2/MeOTf[c]	DCE	>95	3.7	1.0	2.0
4	Me_2S_2/Tf_2O	DCE	>95	3.0	1.0	1.0
5	NCS/TfOH	DCE	>95	5.0	1.0	5.7
6	NIS/TfOH	DCE	>95	5.9	1.0	1.5
7[d]	NIS/TfOH	DCE	41	6.0	1.0	nd
8	NIS/AgOTf	DCE	>95	4.7	1.0	0.6
9	NIS/AgOTf	Et_2O	>95	5.8	1.0	nd
10	**NIS/AgOTf**	**CH_3CN**	**>95 (84)[e]**	**7.9**	**1.0**	**nd**
11[f]	NIS/AgOTf	CH_3CN	>95	nd	nd	1.0
12[f]	NIS/AgOTf	DCE	>95	nd	nd	1.0
13	NIS/$AgClO_4$	CH_3CN	>95	3.2	1.0	nd
14	NIS/$AgBF_4$	CH_3CN	>95	3.2	1.0	nd

[a]Determined by ^{1}H NMR analysis of the crude reaction mixture. [b]Not detected. [c]In situ formed DMTST. [d]Performed at −40 °C. [e]Performed at 1.25 mmol scale. Value in parentheses corresponds to the isolated yield of **15β** and **15α**. [f]Donor and reagents were premixed before the addition of acceptor **9** (preactivation conditions).

Similarly to thioglycosides, β-selectivity was enhanced when the Phen group containing donor **4** was used in comparison with donor **5**, although the formation of glycals **16** and **18** was predominant.

The impact of phenacyl substitution on β-selectivity was also examined. As depicted in Scheme 3, thioglycoside donors **6** and **7**, bearing the methoxy group at positions 3′ and 2′ on the aromatic ring, respectively, as well as previously described donor **2** and unsubstituted donor **8** were coupled with acceptor **9** through the optimized glycosylation conditions, thereby generating Kdo glycosides **15** and **19−21** with yields ranging from 73 to 80%. Owing to the electron-donating properties of the methoxy group, it was anticipated that 4′ and 2′-substituted Phen derivatives **2** and **7** would give the highest β/α ratios on an electronic effect basis. Although this was true for donor **2**, only moderate β-selectivity (4.6:1.0) was obtained with donor **7**. Moreover, similar β/α ratios were obtained for donors **6** and **8** (~6.4:1.0), as expected. These results mean that both electronic and steric effects could be responsible for the formation of the plausible α-spiro intermediate, which accounts for the enhanced β-selectivity.

Having studied various parameters modulating β-selectivity, we next investigated the general scope of the glycosylation reaction. In order to do so, a series of acceptors (Figure 3) featuring primary, secondary, or tertiary alcohols, including 1-nonanol (**10**), cyclohexanol (**11**), 2-adamantanol (**12**), 1-adamantanol (**13**), and methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside (**14**), was reacted with thioglycoside donors **2** and **3** under the optimized conditions, i.e., NIS/AgOTf, CH_3CN, −10 °C (Scheme 4). When 1.4 equiv of acceptors **10−14** was used, the reactions provided Kdo glycosides **22−31** with fair to very good yields (40−87%) while minimizing the formation of glycals **16** and **18**. In all cases, β-Kdo glycosides were formed predominantly with the exception of the glycosylation of donor **3** with 1-adamantanol (**13**), which was moderately α-selective (β/α 1.0:1.6). Once again, the effect of the Phen auxiliary group at C1 significantly enhanced β-selectivity in all cases (up to 2-fold) compared to the nonparticipating benzyl ester. It is worth mentioning that using Phen donor **2** with acceptor **13** led to an inversion in selectivity, giving a slight excess of β-Kdo glycoside **28** (β/α 1.6:1.0). Moreover, glycosylation with 4,6-diol **14** was fully regioselective at the C6 primary position.

Determination of the Anomeric Configuration of Kdo Glycosides. Since Kdo glycosides lack an anomeric proton at the C2 position, determination of anomeric configuration is not as straightforward as it is for other glycosides and cannot rely only on ^{1}H NMR analysis. One of the most accurate methods is the determination of the coupling constant between carbonyl carbon at C1 and axial proton at C3.[49] For Kdo glycosides adopting a $^5C_2$ conformation, which is the case for glycosides **22−31**, a $^3J_{C1,H3ax}$ value of 5.0−7.0 Hz is indicative of a β-configuration while a value ≤1.0 Hz denotes an α-configuration. Thus, the α- or β-anomeric configuration of Kdo glycosides **22−31** was determined via examination of this coupling constant obtained from an undecoupled 150 MHz ^{13}C NMR experiment.

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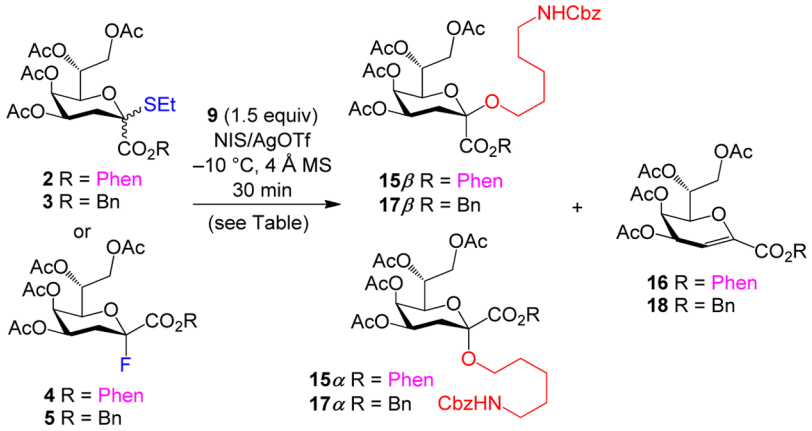
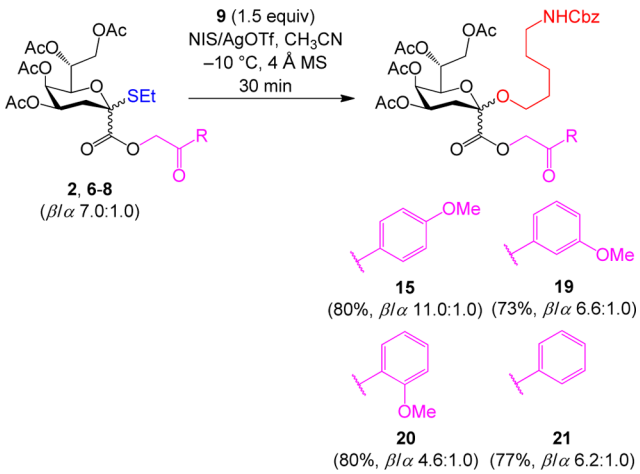
Table 2. Synthesis of β-Kdo Glycosides: Influence of Phenacyl Group and Anomeric Ratio of Donors



entry	donor (β/α ratio)	solvent	conv[a] (%)	selectivity ratio[a] β	α	glycal
1	**3** (1:1)	DCE	90	3.8	1.0	nd[b]
2	**2** (1:1)	DCE	>95	4.7	1.0	0.6
3	**3** (1:1)	CH_3CN	93	3.4	1.0	nd
4	**2** (1:1)	CH_3CN	>95	7.9	1.0	nd
5	**3** (7:1)	DCE	>95	4.8	1.0	nd
6	**2** (7:1)	DCE	>95	10.8	1.0	nd
7	**3** (7:1)	CH_3CN	>95 (94)[c]	6.3	1.0	nd
8	**2 (7:1)**	**CH_3CN**	**>95**	**11.0**	**1.0**	**nd**
9[d]	**3** (7:1)	CH_3CN	>95	3.0	1.0	nd
10[d]	**2** (7:1)	CH_3CN	>95	4.0	1.0	nd
11[e]	**5** (0:1)	DCM	>95	1.0	4.0	1.1
12[e]	**4** (0:1)	DCM	>95	1.0	1.0	1.4

[a]Determined by ^{1}H NMR analysis of the crude reaction mixture. [b]Not detected. [c]Performed at the gram scale. Value in parentheses corresponds to the isolated yield of **17β** and **17α**. [d]IBr was used instead of NIS. [e]Fluoride donors **4** and **5** were activated with $BF_3{\cdot}OEt_2$ (6.0 equiv) and the reaction performed at 0 °C for 2 h.

Scheme 3. Impact of Phenacyl Substitution on β/α Ratio



As expected, $^3J_{C1,H3ax}$ values were found to be between 5.0 and 7.0 Hz for β-glycosides and ≤1.0 Hz for α-glycosides. Furthermore, an interesting empirical observation was made by comparing the ^{1}H NMR data of α- and β-Kdo glycosides. We found that the two geminal protons at C8 were closer (or superimposed) for β-Kdo glycosides, while the differences in the chemical shifts (Δδ) between H-8a and H-8b were more pronounced for α-Kdo glycosides (Δδ from 0.46 to 0.54 ppm). This statement was true for all of the synthesized Kdo glycosides. However, Δδ values between H-3ax and H-3eq were not always smaller for α-glycosides, especially for 1- and 2-adamantyl glycosides **26**−**29**, and thus, as recently emphasized by Mong,[26] this empirical method could not be reliably used for determining the anomeric configuration of Kdo glycosides.

Deprotection of the Phenacyl Group. As previously mentioned, one of the main advantage of using a Phen auxiliary group lies in its possible chemoselective cleavage in the presence of other protecting groups. As examples, Kdo glycosides **22** and **15** were reacted with activated Zn powder in the presence of AcOH at 35 °C for 2 h (Scheme 5) to produce free carboxylic acids **32** and **33** with very good yields (85 and 89%, respectively). The Phen derivatives were thus deprotected chemoselectively in the presence of acetyl and NHCbz groups, showing the orthogonality of this auxiliary functionality. Importantly, other reaction conditions that have not been tested in the course of this study could also be suitable for the selective cleavage of phenacyl groups including $(Bu_3Sn)_2O$ in refluxing DCE; TBAF in THF; H_2, Pd/C; and photodeprotection.[65]

Proposed Mechanism. On the basis of the above experimental results, DFT calculations, and literature precedent,[66] reaction mechanism and plausible intermediates were proposed, accounting for the formation of both α- and β-Kdo glycosides. As shown in Figure 4, NIS would react with AgOTf to form an electrophilic species that would activate Kdo thioglycoside donors **2** or **3**. Following activation, oxocarbenium ion **I** would be formed together with EtSI and a proton acceptor imine. DFT calculations showed that, owing to the highly unstable

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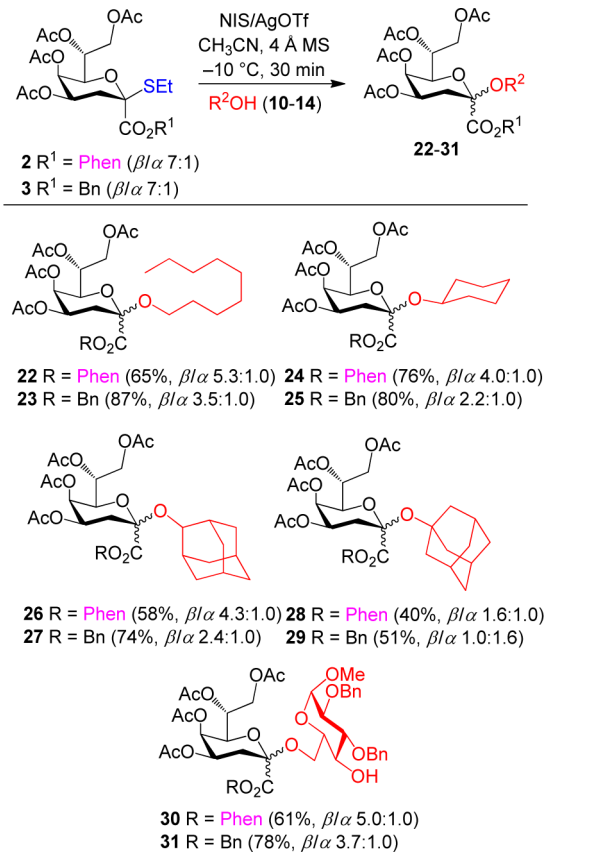
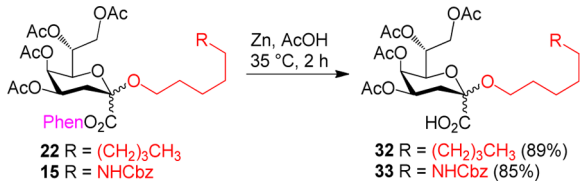
Scheme 4. Scope of the Synthesis of β-Kdo Glycosides Using Different Acceptors



Scheme 5. Zn-Mediated Cleavage of Phenacyl Group



nature of intermediate **I**, it is likely that acetyl group at C4 would stabilize ion **I** from the β-face, thereby forming dioxalenium ion intermediate **II** in the $B_{3,6}$ conformation (Figure S1). α-Triflate **III** would also be a plausible intermediate, which would be stabilized by the electron-withdrawing nature of acetyl groups and carboxylate at C1. Calculations revealed that triflate **III** would exist in the $^5C_2$ conformation and be a stable intermediate. As previously discussed, α-spiroPhen **IV** would be a plausible intermediate, which would be formed by the attack of the Phen activated ketone on the α-face of oxocarbenium ion **I**. For Kdo donors bearing a Phen group, all these intermediates (**I**−**IV**) would exist in equilibrium, reacting in different ways with the acceptor (R^1OH). Glycosylation of oxocarbenium ion **I**, according to the Woerpel model, as well as β-dioxalenium ion **II** would produce α-Kdo glycoside as the major anomer. On the other hand, glycosylation of α-triflate **III** and α-spiroPhen **IV** would occur from the β-face leading to the preferential formation of β-Kdo glycoside. α-Triflate **III** would thus represent a plausible intermediate, accounting for the good β-selectivity obtained with Kdo donor **3** bearing a nonparticipating benzyl ester. Limitations of this mechanistic pathway include difficulties in explaining the impact of the starting anomeric ratio of donors giving enhanced β-selectivity for β-Kdo thioglycosides in comparison with their α-counterparts (retention of configuration). Moreover, we cannot rule out the possibility that the generated *N*-succinimide (NHS) would trap the oxocarbenium ion forming a transient *N*-glycoside that could be displaced by the glycosyl acceptor.[67−70]

CONCLUSIONS

In summary, a novel methodology was developed for the stereoselective formation of β-Kdo glycosides by taking advantage of the long-range participating effect of a 4′-methoxyphenacyl auxiliary group at the C1 position of a peracetylated Kdo thioglycoside donor. In addition to the positive effect of the Phen group, various parameters were shown to be crucial for enhancing the β-selectivity of the reaction, including NIS/AgOTf as promoter, CH_3CN as solvent, β-anomeric configuration of the donor, as well as *para*-substitution of the Phen aromatic ring. The optimized glycosylation conditions were applied to the synthesis of a series of Kdo glycosides, providing good yields and β-selectivity while minimizing the formation of undesirable glycals. Interestingly, chemoselective deprotection of the Phen group was achieved using activated Zn/HOAc, which represents an advantage over previously reported C1 auxiliary groups. α-Triflate and six-membered α-spiroPhen were postulated as plausible intermediates, accounting for the enhanced β-stereoselectivity obtained with Kdo thioglycoside donors bearing nonparticipating (Bn) or participating (Phen) groups at C1. The developed methodology could find application for the synthesis of β-Kdo-containing oligosaccharides from pathogenic bacteria. Work toward this goal is currently in progress in our laboratory.

EXPERIMENTAL SECTION

General Methods. All starting materials and reagents were purchased from commercial sources and used as received without further purification. Air- and water-sensitive reactions were performed in heat gun dried glassware under Ar atmosphere. Moisture-sensitive reagents were introduced via a dry syringe. Anhydrous solvents were supplied over molecular sieves and used as received. Petroleum ether (PE) refers to the 40−60 °C boiling fraction. Powdered 4 Å molecular sieves (MS) were activated before use by heating with a heat gun for ≥5 min under high vacuum. Reactions were monitored by thin-layer chromatography (TLC) with silica gel 60 F_{254} 0.25 mm precoated aluminum foil plates. Compounds were visualized by using UV_{254} and/or orcinol (1 mg·mL^{-1}) in a 10% H_2SO_4(aq) solution and/or Hanessian's stain [2.5 g $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$, 1.0 g Ce-$(NH_4)_4(SO_4)_4\cdot 2H_2O$, 90 mL H_2O, 10 mL H_2SO_4] with heating. Normal-phase flash column chromatography was performed on silica gel 60 Å (15−40 μm). NMR spectra were recorded at 297 K in the indicated solvent ($CDCl_3$ or MeOD) with 400 or 600 MHz instruments, employing standard software provided by the manufacturer. ^1H and ^{13}C NMR spectra were referenced to tetramethylsilane (TMS, $\delta_H = \delta_C = 0.00$ ppm) as internal reference for spectra in $CDCl_3$ and MeOD. Assignments were based on ^1H, ^{13}C, undecoupled ^{13}C, DEPT-135, COSY, HSQC, and HMBC experiments. High-resolution mass spectra (HRMS) were recorded on an ESI-Q-TOF mass spectrometer.

Computational Method. Reaction intermediates were first modeled using the Sparta'10 V1.1.0 software package (Wavefunction, Inc.). For each intermediate, a conformational distribution was generated through stochastic Monte Carlo guided searches at the molecular mechanics (MMFF) level of theory.[71] Conformers within 25 kJ·mol^{-1} of the most stable conformer were subjected to geometry optimizations with Gaussian 09.E01 software.[72] Calculations using DFT with the hybrid B3LYP functional[73,74] and 6-31G(d,p) basis set[75] were performed with IEF-PCM model solvent (CH_3CN).[76] The most stable

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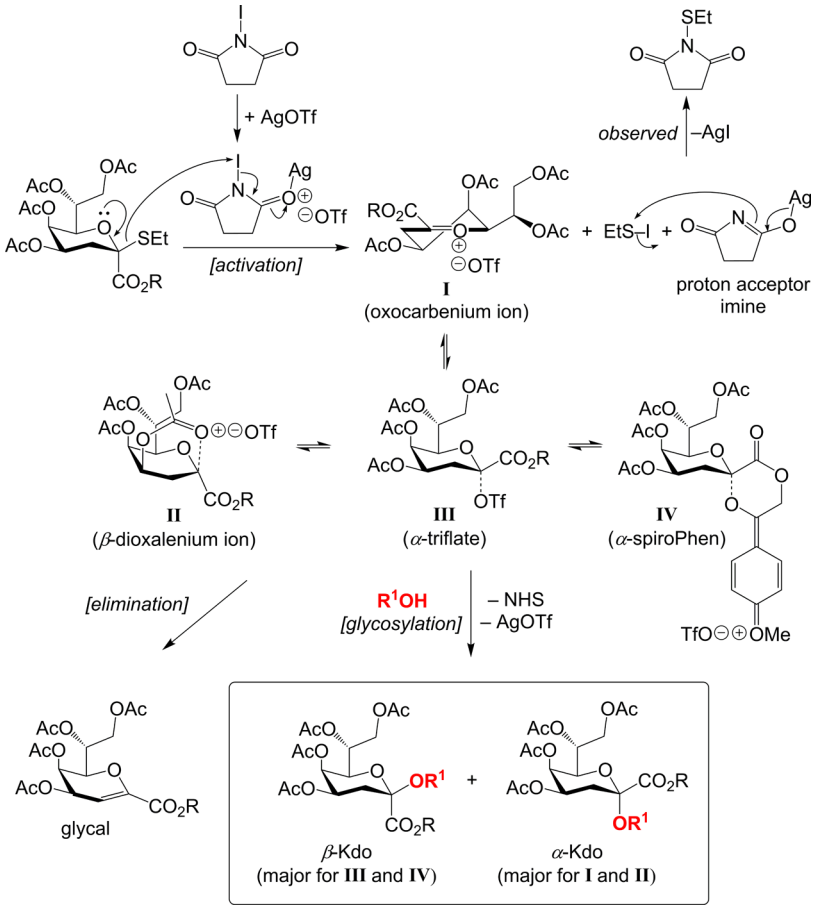

Figure 4. Proposed mechanism and plausible intermediates for the synthesis of β-Kdo glycosides. Dashed lines mean that species can be found either as covalent or contact ion pair intermediates.

conformer of each intermediate was then further optimized at the B3LYP/6-311++G(2d,2p) level of theory.[77,78] In these cases, Grimme's empirical dispersion correction was applied (D3 version).[79] Energy minima were confirmed at 263 K by vibrational analysis at the same level of theory, which also allowed for calculation of the Gibbs free energies. The 3D structures were rendered using PyMOL.

Ammonium 2,4,5,7,8-Penta-O-acetyl-3-deoxy-α-D-manno-oct-2-ulopyranosylonate (1). Crystalline ammonium Kdo[48] (1.39 g, 5.45 mmol, 1.0 equiv) was suspended in anhydrous py (55 mL), and then Ac_2O (55 mL) followed by DMAP (6.6 mg, 54 μmol, 0.01 equiv) were added. The suspension was stirred for 16 h at rt under Ar after which time the solution was found to be homogeneous. The mixture was concentrated under reduced pressure, keeping the temperature below 50 °C, and coevaporated with toluene (3×). The residue was purified by silica gel flash chromatography (DCM/MeOH 1:0 to 6:4) to give peracetylated Kdo (**1**, 2.40 g, 95%, ratio α/β > 95:5) as a yellow oil. The physical and analytical data of **1**[49] were in agreement with those published in the literature.

4′-Methoxyphenacyl (Ethyl 4,5,7,8-tetra-O-acetyl-3-deoxy-2-thio-α,β-D-manno-oct-2-ulopyranosid)onate (2). **Route A.** 2-Bromo-4′-methoxyacetophenone (733 mg, 3.20 mmol, 1.6 equiv), TBAI (111 mg, 301 μmol, 0.15 equiv), and Cs_2CO_3 (1.33 g, 4.08 mmol, 2.0 equiv) were successively added to a solution of peracetylated **1** (900 mg, 2.01 mmol, 1.0 equiv) in anhydrous DMF (20 mL). The mixture was stirred for 16 h at rt under Ar. The suspension was filtered over Celite, rinsed, and diluted with EtOAc (50 mL). The organic phase was washed with a saturated NH_4Cl(aq) solution (25 mL) and H_2O (25 mL). The aqueous phase was back-extracted with EtOAc (25 mL). The combined organic layers were dried over $MgSO_4$, and the solvents were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 8:2 to 6:4) to give 4′-methoxyphenacyl (2,4,5,7,8-penta-*O*-acetyl-3-deoxy-α-D-*manno*-oct-2-ulopyranosyl)-onate (452 mg, 59%) as a white amorphous powder: $[\alpha]_D^{20}$ = +84 (*c* 0.54, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91−7.86 (m, 2H, C*H*-Ar), 6.99−6.95 (m, 2H, C*H*-Ar), 5.46 (d, *J* = 16.0 Hz, 1H, C*H*HPhen), 5.43−5.38 (m, 2H, H-4, H-5), 5.35 (d, *J* = 16.0 Hz, 1H, CH*H*Phen), 5.25 (ddd, $J_{6,7}$ = 9.8 Hz, $J_{7,8b}$ = 3.6 Hz, $J_{7,8a}$ = 2.3 Hz, 1H, H-7), 4.48 (dd, $J_{8a,8b}$ = 12.4 Hz, $J_{7,8a}$ = 2.2 Hz, 1H, H-8a), 4.18 (dd, $J_{6,7}$ = 9.9 Hz, $J_{5,6}$ = 1.0 Hz, 1H, H-6), 4.13 (dd, $J_{8a,8b}$ = 12.4 Hz, $J_{7,8b}$ = 3.6 Hz, 1H, H-8b), 2.49 (dd, $J_{3ax,3eq}$ = 13.1 Hz, $J_{3ax,4}$ = 11.8 Hz, 1H, H-3ax), 2.39 (dd, $J_{3ax,3eq}$ = 13.2 Hz, $J_{3eq,4}$ = 5.1 Hz, 1H, H-3eq), 2.17, 2.12, 2.05, 2.02, 2.00 (all s, 15H, 5 × $COCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.7 (CH_2CO), 170.5, 170.2, 170.1, 169.5, 167.9 (5 × $COCH_3$), 165.8 (C-1), 164.3 (C-Ar), 130.1, 130.0 (CH-Ar), 127.0 (C-Ar), 114.2, 114.2 (CH-Ar), 97.3 (C-2), 69.5 (C-6), 67.3 (C-7), 66.6 (CH_2CO), 65.9 (C-4), 63.9 (C-5), 62.1 (C-8), 55.6 (OCH_3), 31.6 (C-3), 20.7, 20.7, 20.6, 20.6, 20.6 (5 × $COCH_3$); HRMS (ESI-TOF) *m/z* $[M + NH_4]^+$ calcd for $C_{27}H_{36}NO_{15}$ 614.2082, found 614.2079; *m/z* $[M + Na]^+$ calcd for $C_{27}H_{32}NaO_{15}$ 619.1633, found 619.1635. Ethanethiol (12 μL, 170 μmol, 2.0 equiv) was added to a solution of the latter phenacyl (50 mg, 84 μmol, 1.0 equiv) in anhydrous DCM (1.7 mL). The solution was cooled to 0 °C, and then $BF_3{\cdot}OEt_2$ (16 μL, 130 μmol, 1.5 equiv) was added. The mixture was stirred for 24 h under Ar while gradually being warmed to rt. The solution was diluted with DCM, and a saturated $NaHCO_3$(aq) solution was added for neutralization. Then iodine was added until a dark color persisted. The excess iodine was reduced by washing the organic phase with a freshly prepared 10% $Na_2S_2O_3$(aq) solution until the red color disappeared. The solution was poured into a separatory funnel, and the aqueous layer was extracted with DCM. The pooled organic phases were dried over $MgSO_4$ and filtered, and the solvents were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 1:0 to 5:55) to give thioglycoside **2** (13 mg, 25%) in a 9.0:1.0 β/α anomeric mixture: $[\alpha]_D^{20}$ = +50 (*c* 0.83, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, β-anomer) δ 7.93−7.87 (m, 2H,

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C*H*-Ar), 6.95 (m, 2H, C*H*-Ar), 5.54−5.38 (m, 3H, C*H*HPhen, H-4, H-5), 5.37−5.28 (m, 1H, CH*H*Phen), 5.28−5.20 (m, 1H, H-7), 4.36−4.33 (m, 2H, H-8a, H-8b), 4.24 (dd, $J_{6,7}$ = 9.6 Hz, $J_{5,6}$ = 1.1 Hz, 1H, H-6), 3.89 (s, 3H, OCH_3), 2.91−2.77 (m, 1H, SC*H*H), 2.74−2.66 (m, 1H, SCH*H*), 2.63 (dd, $J_{3eq,3ax}$ = 12.6 Hz, $J_{3eq,4}$ = 4.2 Hz, 1H, H-3eq), 2.23 (t, $J_{3ax,3eq} \approx J_{3ax,4}$ = 12.9 Hz, 1H, H-3ax), 2.13, 2.03, 1.99, 1.97 (s, 12H, 4 × COCH_3), 1.26 (t, *J* = 7.5 Hz, 3H, SCH_2CH_3); ^{1}H NMR (400 MHz, $CDCl_3$, *α*-anomer) *δ* 7.93−7.87 (m, 2H, C*H*-Ar), 6.95 (m, 2H, C*H*-Ar), 5.54−5.38 (m, 3H, C*H*HPhen, H-4, H-5), 5.37−5.28 (m, 1H, CH*H*Phen), 5.28−5.20 (m, 1H, H-7), 4.63 (dd, $J_{8a,8b}$ = 12.3 Hz, $J_{7,8a}$ = 2.4 Hz, 1H, H-8a), 4.53 (dd, $J_{6,7}$ = 9.7 Hz, $J_{5,6}$ = 1.3 Hz, 1H, H-6), 4.12 (dd, $J_{8a,8b}$ = 12.3 Hz, $J_{7,8b}$ = 3.6 Hz, 1H, H-8b), 3.89 (s, 3H, OCH_3), 2.91−2.77 (m, 1H, SC*H*H), 2.59−2.53 (m, 1H, SCH*H*), 2.50 (dd, $J_{3ax,3eq}$ = 11.9 Hz, $J_{3ax,4}$ = 10.6 Hz, 1H, H-3ax), 2.33 (dd, $J_{3ax,3eq}$ = 13.7 Hz, $J_{3eq,4}$ = 4.8 Hz, 1H, H-3eq), 2.10, 2.08, 2.03, 2.01, (s, 12H, 4 × COCH_3), 1.26 (t, *J* = 7.5 Hz, 3H, SCH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$, *β*-anomer) *δ* 189.3 (*C*O), 170.8, 170.6, 169.9, 169.7 (4 × *C*OCH$_3$), 167.8 (C-1), 164.3 (C-Ar), 130.1 (*C*H-Ar), 126.7 (C-Ar), 114.2 (*C*H-Ar), 83.9 (C-2), 72.1 (C-6), 67.9 (C-7), 67.2 (C-4), 66.9 (*C*H$_2$), 64.4 (C-5), 62.5 (C-8), 55.6 (O*C*H$_3$), 32.8 (C-3), 22.6 (S*C*H$_2$*β*), 20.8−20.7 (4 × *C*OCH$_3$), 14.1 (S*C*H$_2$*C*H$_3$); ^{13}C NMR (100 MHz, $CDCl_3$, *α*-anomer) *δ* 189.6 (*C*O), 170.5, 170.4, 169.9, 169.7 (4 × *C*OCH$_3$), 167.7 (C-1), 164.2 (C-Ar), 130.1 (*C*H-Ar), 127.0 (C-Ar), 114.2 (*C*H-Ar), 85.1 (C-2), 68.3 (C-6), 67.6 (C-7), 67.0 (C-4), 66.6 (*C*H$_2$), 64.4 (C-5), 61.9 (C-8), 55.6 (O*C*H$_3$), 31.9 (C-3), 23.5 (S*C*H$_2$), 20.8−20.7 (4 × *C*OCH$_3$), 13.6 (S*C*H$_2$*C*H$_3$); HRMS (ESI-TOF) *m/z* [M + H]$^+$ calcd for $C_{27}H_{35}O_{13}S$ 599.1793, found 599.1789; *m/z* [M + NH$_4$]$^+$ calcd for $C_{27}H_{38}NO_{13}S$ 616.2058, found 616.2059; *m/z* [M + Na]$^+$ calcd for $C_{27}H_{34}NaO_{13}S$ 621.1612, found 621.1611. **Route B.** Ethanethiol (261 *μ*L, 3.53 mmol, 5.0 equiv) was added to a solution of peracetylated **1**[49] (328 mg, 705 *μ*mol, 1.0 equiv) in anhydrous DCE (7.1 mL) at rt under Ar. The solution was cooled to 0 °C, and BF$_3$·OEt$_2$ (183 *μ*L, 1.48 mmol, 2.1 equiv) was slowly added. The mixture was refluxed for 40 min and then cooled at rt prior to addition of Et$_3$N (206 *μ*L, 1.48 mmol, 2.1 equiv). The solvents were concentrated under reduced pressure to give a residue that was used in the next step without further purification. 2-Bromo-4′-methoxyacetophenone (322 mg, 1.41 mmol, 2.0 equiv) was added to a solution of the crude thioglycoside in anhydrous DMF (5.6 mL) followed by Cs$_2$CO$_3$ (69 mg, 210 *μ*mol, 0.3 equiv), and the mixture was stirred for 2 h at rt under Ar. The suspension was filtered over Celite, rinsed, and diluted with EtOAc (50 mL). The organic phase was washed with a saturated NH$_4$Cl(aq) solution (25 mL) and H$_2$O (25 mL). The combined organic layers were dried over MgSO$_4$, and the solvents were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 9:1 to 6:4) to give thioglycoside **6** (190 mg, 45%, two steps) as a yellow oil in a ∼1:1 *β*/*α* anomeric mixture.

Route C: Representative Procedure for the Synthesis of Phenacyl Derivatives starting from Benzyl Ester 3. Thioglycoside **3** (965 mg, 1.79 mmol, 1.0 equiv, ratio *β*/*α* 7:1) was dissolved in anhydrous DCE/MeOH (35 mL, 1:4 v/v). The solution was degassed with Ar, and 10% Pd/C (965 mg) was added. The suspension was stirred under an atmosphere of H$_2$ at rt for 2 h. The mixture was filtered over Celite to remove the catalyst, and the cake was rinsed with MeOH and DCM. The solvents were concentrated under reduced pressure to give a residue (804 mg, quant) as a yellow oil, which was used in the next step without further purification. 2-Bromo-4′-methoxyacetophenone (61 mg, 270 *μ*mol, 1.5 equiv) was added to a solution of crude carboxylic acid (80 mg, 180 *μ*mol) in anhydrous DMF (0.9 mL) followed by Cs$_2$CO$_3$ (64 mg, 200 *μ*mol, 1.1 equiv). The mixture was stirred for 2 h at rt under Ar. The suspension was filtered over Celite, rinsed, and diluted with EtOAc (100 mL). The organic phase was washed with a saturated NH$_4$Cl(aq) solution (50 mL) and H$_2$O (50 mL). The combined organic layers were dried over MgSO$_4$, and the solvents were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 1:0 to 6:4) to give thioglycoside **2** (81 mg, 76%) as a colorless oil in a 7:1 *β*/*α* anomeric mixture.

Benzyl (Ethyl 4,5,7,8-tetra-O-acetyl-3-deoxy-2-thio-α,β-D-manno-oct-2-ulopyranosid)onate (3). **Route A.** BnBr (848 *μ*L, 7.09 mmol, 2.2 equiv) followed by Cs$_2$CO$_3$ (420 mg, 1.29 mmol, 0.4 equiv) were added to a solution of peracetylated **1**[49] (1.5 g, 3.2 mmol, 1.0 equiv) in anhydrous DMF (16 mL). The mixture was stirred for 2 h at rt under Ar. The suspension was filtered over Celite, rinsed, and diluted with EtOAc (50 mL). The organic phase was washed with a saturated NH$_4$Cl(aq) solution (25 mL) and H$_2$O (25 mL). The combined organic layers were dried over MgSO$_4$, and the solvents were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 8:2 to 7:3) to give benzyl (2,4,5,7,8-penta-*O*-acetyl-3-deoxy-*α*-D-*manno*-oct-2-ulopyranosyl)onate (1.26 g, 73%) as a white foam. The physical and analytical data of the latter compound[80] were in agreement with those published in the literature. Ethanethiol (286 *μ*L, 3.86 mmol, 2.0 equiv) was added to a solution of the benzyl ester (1.04 g, 1.93 mmol, 1.0 equiv) in anhydrous DCE (10 mL). The solution was cooled to 0 °C, and then BF$_3$·OEt$_2$ (357 *μ*L, 2.90 mmol, 1.5 equiv) was slowly added. The mixture was stirred for 2 h under Ar while gradually being warmed to rt. The solution was diluted with DCM, and a saturated NaHCO$_3$(aq) solution was added for neutralization. Then, iodine was added until a dark color persisted. The excess of iodine was reduced by washing the organic phase with a freshly prepared 10% Na$_2$S$_2$O$_3$(aq) solution until the red color disappeared. The solution was poured into a separatory funnel, and the aqueous layer was extracted with DCM. The pooled organic phases were dried over MgSO$_4$ and filtered, and the solvents were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 85:15 to 75:25) to give thioglycoside **3** (956 mg, 92%) as a 7.0:1.0 *β*/*α* anomeric mixture. The physical and analytical data of **3**[10] were in agreement with those published in the literature. **Route B.** Ethanethiol (307 *μ*L, 4.14 mmol, 5.0 equiv) was added to a solution a peracetylated **1**[49] (386 mg, 829 *μ*mol, 1.0 equiv) in anhydrous DCE (8.0 mL) at rt under Ar. The solution was cooled to 0 °C, and BF$_3$·OEt$_2$ (95 *μ*L, 770 *μ*mol, 2.0 equiv) was slowly added. The mixture was refluxed for 40 min and then cooled at rt prior to addition of Et$_3$N (230 *μ*L, 4.15 mmol, 5.0 equiv). The solvents were concentrated under reduced pressure to give a residue that was used in the next step without further purification. Benzyl bromide (218 *μ*L, 1.82 mmol, 2.2 equiv) was added to a solution of the crude thioglycoside in anhydrous DMF (4.1 mL) followed by Cs$_2$CO$_3$ (108 mg, 332 *μ*mol, 0.4 equiv), and the mixture was stirred for 2 h at rt under Ar. The suspension was filtered over Celite, rinsed, and diluted with EtOAc (50 mL). The organic phase was washed with a saturated NH$_4$Cl(aq) solution (25 mL) and H$_2$O (25 mL). The combined organic layers were dried over MgSO$_4$, and the solvents were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 9:1 to 6:4) to give thioglycoside **3** (224 mg, 50%, two steps) as a yellow oil in a ∼1:1 *β*/*α* anomeric mixture.

4′-Methoxyphenacyl (Fluoride 4,5,7,8-tetra-O-acetyl-3-deoxy-α-D-manno-oct-2-ulopyranosyl)onate (4). HF·py (5.0 mL, ca. 70% HF, ca. 30% py) was added to a solution of peracetylated **1**[49] (675 mg, 1.59 mmol, 1.0 equiv) in anhydrous DCM (16 mL) at 0 °C under Ar. The mixture was stirred for 3 h while gradually being warmed to rt. Ice-cold water (10 mL) was added, and the phases were mixed and left separated. The aqueous phase was acidified with 10% HCl(aq) until pH ∼ 3 and extracted with DCM (3 × 10 mL). The combined organic layers were dried over MgSO$_4$ and filtered, and the solvents were concentrated under reduced pressure to give a crude fluoride (391 mg, 63%) as a colorless oil after being placed under high vacuum for 3 h. A portion of the latter compound (191 mg, 450 *μ*mol, 1.0 equiv) was dissolved in anhydrous DMF (2.3 mL). 2-Bromo-4′-methoxyacetophenone (226 mg, 989 *μ*mol, 2.2 equiv) followed by Cs$_2$CO$_3$ (59 mg, 180 *μ*mol, 0.4 equiv) were added, and the mixture was stirred for 2 h at rt under Ar. The suspension was filtered over Celite, rinsed, and diluted with EtOAc (50 mL). The organic phase was washed with a saturated NH$_4$Cl(aq) solution (25 mL) and H$_2$O (25 mL). The combined organic layers were dried over MgSO$_4$, and the solvents were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 1:0 to 6:4) to give *α*-fluoride **4** (192 mg, 77%) as a yellow oil: $[\alpha]_D^{20}$ = +35 (*c* 0.75, CHCl$_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.91−7.87 (m, 2H, C*H*-Ar), 7.00−6.96 (m, 2H, C*H*-Ar), 5.51−5.44 (m, 3H, H-5, C*H*$_2$Phen), 5.39 (ddd, $J_{3ax,4}$ = 12.1 Hz, $J_{4,5}$ = 5.4 Hz, $J_{3eq,4}$ = 3.0 Hz, 1H, H-4), 5.26 (dddd, $J_{6,7}$ = 9.6 Hz, $J_{7,8b}$ = 4.4 Hz, $J_{7,8a}$ = 2.3 Hz, $J_{5,7}$ = 0.8 Hz, 1H, H-7), 4.51 (dd, $J_{8a,8b}$ = 12.4 Hz, $J_{7,8a}$ = 2.3 Hz, 1H, H-8a), 4.42 (dd, $J_{6,7}$ = 9.7 Hz, $J_{5,6}$ = 1.3 Hz, 1H, H-6), 4.17 (dd, $J_{8a,8b}$ = 12.4 Hz, $J_{7,8b}$ =

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4.4 Hz, 1H, H-8b), 3.89 (s, 3H, OCH_3), 2.63−2.41 (m, 2H, H-3ax, H-3eq), 2.12, 2.09, 2.02, 2.02 (all s, 12H, 4 × $COCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.9 (COPhen), 170.7, 170.5, 170.0, 169.8 (4 × $COCH_3$), 164.3 (C-1, $^2J_{C1,F}$ = 41.8 Hz), 130.2 (2 × CH-Ar), 126.9 (C-Ar), 114.4 (2 × CH-Ar), 108.3 (C-2, $^1J_{C2,F}$ = 232 Hz), 70.7 (C-6, $^3J_{C6,F}$ = 1.5 Hz), 67.5 (C-7), 67.1 (CH_2Phen), 65.6 (C-4), 64.1 (C-5), 62.2 (C-8), 55.7 (OCH_3), 30.7 (C-3, $^2J_{C3,F}$ = 27.3 Hz), 20.84 (2C), 20.78, 20.77 (4 × $COCH_3$); ^{19}F (376 MHz, $CDCl_3$) δ 376.5 (dd, $^3J_{F,H3ax}$ = 34.6 Hz, $^3J_{F,3eq}$ = 6.0 Hz); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{25}H_{29}FNaO_{13}$ 579.1484, found 579.1494.

*Benzyl (Fluoride 4,5,7,8-tetra-O-acetyl-3-deoxy-α-D-manno-oct-2-ulopyranosyl)onate (**5**).* HF·py (5.0 mL, ca. 70% HF, ca. 30% py) was added to a solution of peracetylated **1**[49] (675 mg, 1.59 mmol, 1.0 equiv) in anhydrous DCM (16 mL) at 0 °C under Ar. The mixture was stirred for 3 h while gradually being warmed to rt. Ice-cold water (10 mL) was added, and the phases were mixed and left separated. The aqueous phase was acidified with 10% HCl(aq) until pH ∼ 3 and extracted with DCM (3 × 10 mL). The combined organic layers were dried over $MgSO_4$ and filtered, and the solvents were concentrated under reduced pressure to give a crude fluoride (391 mg, 63%) as a colorless oil after being placed under high vacuum for 3 h. A portion of the latter compound (191 mg, 450 μmol, 1.0 equiv) was dissolved in anhydrous DMF (2.3 mL). BnBr (118 μL, 989 μmol, 2.2 equiv) followed by Cs_2CO_3 (59 mg, 180 μmol, 0.4 equiv) were added, and the mixture was stirred for 2 h at rt under Ar. The suspension was filtered over Celite, rinsed, and diluted with EtOAc (50 mL). The organic phase was washed with a saturated NH_4Cl(aq) solution (25 mL) and H_2O (25 mL). The organic layer was dried over $MgSO_4$, and the solvents were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 1:0 to 55:45) to give α-fluoride **5** (159 mg, 71%) as a colorless oil: $[\alpha]_D^{20}$ = +50 (*c* 1.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44−7.33 (m, 5H, C*H*-Ar), 5.44−5.42 (m, 1H, H-5), 5.33 (ddd, $J_{3ax,4}$ = 11.9 Hz, $J_{4,5}$ = 5.4 Hz, $J_{3eq,4}$ = 3.0 Hz, 1H, H-4), 5.29 (d, *J* = 10.1 Hz, 1H, C*H*HPh), 5.28 (d, *J* = 9.4 Hz, 1H, CH*H*Ph), 5.21 (dddd, $J_{6,7}$ = 9.7 Hz, $J_{7,8b}$ = 4.4 Hz, $J_{7,8a}$ = 2.3 Hz, $J_{5,7}$ = 1.0 Hz, 1H, H-7), 4.49 (dd, $J_{8a,8b}$ = 12.3 Hz, $J_{7,8a}$ = 2.3 Hz, 1H, H-8a), 4.38 (dd, $J_{6,7}$ = 9.7 Hz, $J_{5,6}$ = 1.3 Hz, 1H, H-6), 4.13 (dd, $J_{8a,8b}$ = 12.3 Hz, $J_{7,8b}$ = 4.4 Hz, 1H, H-8b), 2.44−2.23 (m, 2H, H-3ax, H-3eq), 2.10, 2.07, 2.01, 2.00 (all s, 12H, 4 × $COCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 170.4, 169.9, 169.8 (4 × $COCH_3$), 164.4 (C-1, $^2J_{C1,F}$ = 29.7 Hz), 134.7 (C-Ar), 128.9, 128.8, 128.3 (5 × CH-Ar), 108.1 (C-2, $^1J_{C2,F}$ = 232 Hz), 70.7 (C-6, $^3J_{C6,F}$ = 2.2 Hz), 68.2 (CH_2Ph), 67.4 (C-7), 65.7 (C-4), 64.1 (C-5), 62.2 (C-8), 30.3 (C-3, $^2J_{C3,F}$ = 27.6 Hz), 20.82 (2C), 20.77, 20.7 (4 × $COCH_3$); ^{19}F NMR (376 MHz, $CDCl_3$) δ 376.5 (dd, $^3J_{F,H3ax}$ = 34.1 Hz, $^3J_{F,H3eq}$ = 5.4 Hz); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{23}H_{27}FNaO_{11}$ 521.1430, found 521.1421; *m/z* [2 M + Na]$^+$ calcd for $C_{46}H_{54}F_2NaO_{22}$ 1019.2967, found 1019.2944.

*3′-Methoxyphenacyl (Ethyl 4,5,7,8-tetra-O-acetyl-3-deoxy-2-thio-α,β-D-manno-oct-2-ulopyranosid)onate (**6**).* Thioglycoside **3** (β/α 7:1, 163 mg, 303 μmol, 1.0 equiv) was reacted according to the representative procedure for the synthesis of phenacyl derivatives starting from benzyl ester **3** and gave thioglycoside **6** (147 mg, 81%, two steps, β/α 7:1) as a white foam: $[\alpha]_D^{20}$ = +74 (*c* 0.23, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, β-anomer) δ 7.49−7.45 (m, 2H, C*H*-Ar), 7.44−7.39 (m, 1H, C*H*-Ar), 7.20−7.16 (m, 1H, C*H*-Ar), 5.54 (d, *J* = 16.2 Hz, 1H, C*H*HPhen), 5.48−5.41 (m, 2H, H-5, H-4), 5.37 (d, *J* = 16.2 Hz, 1H, CH*H*Phen), 5.23 (ddd, $J_{6,7}$ = 9.6 Hz, $J_{7,8b}$ = 5.2 Hz, $J_{7,8a}$ = 2.9 Hz, 1H, H-7), 4.36−4.33 (m, 2H, H-8a, H-8b), 4.22 (d, $J_{6,7}$ = 9.6 Hz, $J_{5,6}$ = 1.0 Hz, 1H, H-6), 3.87 (s, 3H, OCH_3), 2.91−2.81 (m, 1H, SC*H*H), 2.73−2.66 (m, 1H, SCH*H*), 2.63 (ddd, $J_{3ax,3eq}$ = 12.5 Hz, $J_{3eq,4}$ = 4.2 Hz, $J_{3eq,5}$ = 0.9 Hz, 1H, H-3eq), 2.24 (t, $J_{3ax,3eq} \approx J_{3ax,4} \approx$ 12.5 Hz, 1H, H-3ax), 2.13, 2.03, 2.00, 1.98 (all s, 12H, 4 × $COCH_3$), 1.27 (t, *J* = 7.6 Hz, 3H, SCH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$, β-anomer) δ 190.9 (COPhen), 170.9, 169.9, 169.8, 167.9 (4 × $COCH_3$), 167.9 (C-1), 160.3, 135.2 (2 × C-Ar), 130.1, 121.0, 120.3, 112.1 (4 × CH-Ar), 84.1 (C-2), 72.3 (C-6), 68.1 (C-7), 67.4 (C-4), 67.3 (CH_2Phen), 64.5 (C-5), 62.7 (C-8), 55.7 (OCH_3), 33.0 (C-3), 23.6 (SCH_2), 20.9−20.8 (4 × $COCH_3$), 14.2 (SCH_2CH_3); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{27}H_{34}NaO_{13}S$ 621.1612, found 621.1618; *m/z* [2 M + Na]$^+$ calcd for $C_{54}H_{68}NaO_{26}S_2$ 1219.3332, found 129.3336.

*2′-Methoxyphenacyl (Ethyl 4,5,7,8-tetra-O-acetyl-3-deoxy-2-thio-α,β-D-manno-oct-2-ulopyranosid)onate (**7**).* Thioglycoside **3** (β/α 7:1, 150 mg, 279 μmol, 1.0 equiv) was reacted according to the representative procedure for the synthesis of phenacyl derivatives starting from benzyl ester **3** and gave thioglycoside **7** (134 mg, 80%, two steps, β/α 7:1) as a white foam: $[\alpha]_D^{20}$ = +52 (*c* 0.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, β-anomer) δ 8.03−8.00 (m, 1H, C*H*-Ar), 7.58−7.53 (m, 1H, C*H*-Ar), 7.09−6.99 (m, 2H, C*H*-Ar), 5.48−5.43 (m, 2H, H-5, H-4), 5.41 (d, *J* = 17.1 Hz, 1H, C*H*HPhen), 5.32 (d, *J* = 17.1 Hz, 1H, CH*H*Phen), 5.26−5.20 (m, 1H, H-7), 4.36−4.34 (m, 2H, H-8a, H-8b), 4.26 (dd, $J_{6,7}$ = 9.6 Hz, $J_{5,6}$ = 1.1 Hz, 1H, H-6), 3.98 (s, 3H, OCH_3), 2.93−2.83 (m, 1H, SC*H*H), 2.77−2.67 (m, 1H, SCH*H*), 2.63 (ddd, $J_{3ax,3eq}$ = 12.5 Hz, $J_{3eq,4}$ = 4.6 Hz, $J_{3eq,5}$ = 1.0 Hz, 1H, H-3eq), 2.22 (t, $J_{3ax,3eq} \approx J_{3ax,4} \approx$ 12.5 Hz, 1H, H-3ax), 2.13, 2.03, 1.99 (all s, 12H, 4 × $COCH_3$), 1.27 (t, *J* = 7.5 Hz, 3H, SCH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$, β-anomer) δ 191.6 (COPhen), 170.9, 170.7, 170.0, 169.8 (4 × $COCH_3$), 168.0 (C-1), 159.8 (C-Ar), 135.4, 131.5 (2 × CH-Ar), 123.9 (C-Ar), 121.3, 111.7 (2 × CH-Ar), 84.2 (C-2), 72.2 (C-6), 71.2 (CH_2Phen), 68.1 (C-7), 67.4 (C-4), 64.6 (C-5), 62.8 (C-8), 55.8 (OCH_3), 33.0 (C-3), 23.6 (SCH_2CH_3), 20.9−20.8 (4 × $COCH_3$), 14.2 (SCH_2CH_3); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{27}H_{34}NaO_{13}S$ 621.1612, found 621.1622; *m/z* [2 M + Na]$^+$ calcd for $C_{54}H_{68}NaO_{26}S_2$ 1219.3332, found 1219.3340.

*Phenacyl (Ethyl 4,5,7,8-tetra-O-acetyl-3-deoxy-2-thio-α,β-D-manno-oct-2-ulopyranosid)onate (**8**).* Thioglycoside **3** (β/α 7:1, 174 mg, 322 μmol, 1.0 equiv) was reacted according to the representative procedure for the synthesis of phenacyl derivatives starting from benzyl ester **3** and gave thioglycoside **8** (129 mg, 70%, two steps, β/α 7:1) as a white foam: $[\alpha]_D^{20}$ = +58 (*c* 0.35, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, β-anomer) δ 7.95−7.91 (m, 2H, C*H*-Ar), 7.67−7.62 (m, 1H, C*H*-Ar), 7.55−7.49 (m, 2H, C*H*-Ar), 5.55 (d, *J* = 16.2 Hz, 1H, C*H*HPhen), 5.48−5.43 (m, 2H, H-5, H-4), 5.39 (d, *J* = 16.2 Hz, 1H, CH*H*Phen), 5.23 (ddd, $J_{6,7}$ = 9.5 Hz, $J_{7,8b}$ = 3.9 Hz, $J_{7,8a}$ = 2.8 Hz, 1H, H-7), 4.36−433 (m, 2H, H-8a, H-8b), 4.22 (dd, $J_{6,7}$ = 9.6 Hz, $J_{5,6}$ = 1.0 Hz, 1H, H-6), 2.91−2.81 (m, 1H, SC*H*H), 2.73−2.65 (m, 1H, SCH*H*), 2.64 (ddd, $J_{3ax,3eq}$ = 12.5 Hz, $J_{3eq,4}$ = 4.2 Hz, $J_{3eq,5}$ = 1.0 Hz, 1H, H-3eq), 2.24 (t, $J_{3ax,3eq} \approx J_{3ax,4} \approx$ 12.5 Hz, 1H, H-3ax), 2.13, 2.03, 2.00, 1.98 (all s, 12H, 4 × $COCH_3$), 1.27 (t, *J* = 7.6 Hz, 3H, SCH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$, β-anomer) δ 191.1 (COPhen), 170.9, 170.7, 170.0, 169.8 (4 × $COCH_3$), 167.9 (C-1), 134.4 (CH-Ar), 133.9 (C-Ar), 129.1 (2C), 127.9 (2C, 4 × CH-Ar), 84.1 (C-2), 72.3 (C-6), 68.1 (C-7), 67.4 (C-4), 67.2 (CH_2Phen), 64.5 (C-5), 62.7 (C-8), 33.0 (C-3), 23.6 (SCH_2), 20.90, 20.89, 20.85, 20.80 (4 × $COCH_3$), 14.2 (SCH_2CH_3); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{26}H_{32}NaO_{12}S$ 591.1507, found 591.1508; *m/z* [2 M + Na]$^+$ calcd for $C_{52}H_{64}NaO_{24}S_2$ 1159.3121, found 1159.3117.

General Procedure for Glycosylation with Thioglycoside Donors. Freshly activated powdered 4 Å molecular sieves (4 mg·mg^{-1} of acceptor) were added to a solution of thioglycoside **2** or **3** (1 equiv), glycosyl acceptor **9**−**14** (1.4−2.0 equiv), and NIS (2.0 equiv) in anhydrous CH_3CN (20 mL·mmol^{-1}). The mixture was stirred for 1 h at rt under Ar. The suspension was then cooled to −10 °C, the flask was protected from light, and AgOTf (1.0 equiv) was added in one portion. The mixture was stirred for 30 min at −10 °C under Ar. Et_3N (2.0 equiv) was added to quench the reaction. The suspension was filtered over Celite and rinsed with DCM, and the solvents were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography to give a mixture of Kdo glycoside anomers.

General Procedure for Glycosylation with Fluoride Donors. Freshly activated powdered 4 Å molecular sieves (4 mg·mg^{-1} of acceptor) were added to a solution of fluoride **4** or **5** (1 equiv) and acceptor **9** (2.0 equiv) in anhydrous DCM (25 mL·mmol^{-1}). The mixture was stirred for 1 h at rt under Ar, and then the suspension was cooled to 0 °C and BF_3·OEt_2 (6.0 equiv) was slowly added. The mixture was stirred from 0 °C to rt for 2 h or until TLC showed complete conversion of the donor. Then the suspension was filtered over Celite, rinsed, and diluted with DCM. The organic phase was washed with a saturated $NaHCO_3$(aq) solution and brine. The organic phase was dried over $MgSO_4$ and filtered, and the solvents were concentrated under reduced pressure. The residue was purified by silica gel flash

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chromatography to give a mixture of Kdo glycoside anomers together with glycal.

*4′-Methoxyphenacyl [2-[5-Amino-N-[(benzyloxy)carbonyl]-1-pentyl] 4,5,7,8-tetra-O-acetyl-3-deoxy-α,β-D-manno-oct-2-ulopyranosid]onate (**15β** and **15α**) and 4′-Methoxyphenacyl 4,5,7,8-Tetra-O-acetyl-2,6-anhydro-3-deoxy-D-manno-oct-2-enosonate (**16**).* Thioglycoside **2** (750 mg, 1.25 mmol, 1.0 equiv, $\beta/\alpha \sim 1{:}1$) and acceptor **9** (595 mg, 2.51 mmol, 2.0 equiv) were reacted according to the general procedure for glycosylation with thioglycoside donors and gave **15** (827 mg, 84%, β/α 7.9:1.0) as a colorless oil: $[\alpha]_D^{20} = -11$ (*c* 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, β-anomer) δ 7.92−7.86 (m, 2H, C*H*-Ar), 7.38−7.28 (m, 5H, C*H*-Ar), 6.98−6.92 (m, 2H, C*H*-Ar), 5.44 (d, *J* = 16.0 Hz, 1H, C*H*HPhen), 5.40−5.38 (m, 1H, H-5), 5.38 (d, *J* = 16.0 Hz, 1H, CH*H*Phen), 5.32 (ddd, $J_{3ax,4}$ = 13.0 Hz, $J_{3eq,4}$ = 4.6 Hz, $J_{4,5}$ = 3.0 Hz, 1H, H-4), 5.21 (ddd, $J_{6,7}$ = 13.0 Hz, $J_{7,8a}$ = 4.6 Hz, $J_{7,8b}$ = 3.0 Hz, 1H, H-7), 5.11−5.07 (m, 2H, COCH_2Ph), 5.02−4.93 (m, 1H, N*H*Cbz), 4.42−4.29 (m, 3H, H-8a, H-8b, H-6), 3.82 (dt, *J* = 9.2, 6.3 Hz, 1H, H-1a′), 3.52 (dt, *J* = 9.2, 6.3 Hz, 1H, H-1b′), 3.24−3.18 (m, 2H, H-5ab′), 2.52 (dd, $J_{3eq,3ax}$ = 12.5 Hz, $J_{3eq,4}$ = 4.7 Hz, 1H, H-3eq), 2.16 (t, $J_{3eq,3ax} \approx J_{3ax,4} \approx$ 12.8 Hz, 1H, H-3ax), 2.11, 2.02, 2.00, 1.99 (all s, 12H, 4 × COCH_3), 1.68−1.51 (m, 4H, H-2ab′, H-4ab′), 1.47−1.37 (m, 2H, H-3ab′); ^{13}C NMR (100 MHz, $CDCl_3$, β-anomer) δ 189.1 (COPhen), 170.8, 170.5, 169.9, 169.7 (4 × $COCH_3$), 167.5 (C-1, $^3J_{C1,H3ax}$ = 5.2 Hz), 164.3 ($COCH_2$Ph), 156.5 (C-Ar), 136.7 (C-Ar), 130.1, 128.5, 128.0 (CH-Ar), 126.7 (C-Ar), 114.2 (CH-Ar), 99.5 (C-2), 70.8 (C-6), 68.1 (C-7), 67.2 (C-4), 66.6, 66.5 (2 × CH_2), 64.4 (C-1′), 64.3 (C-5), 62.7 (C-8), 55.6 (OCH_3), 40.9 (C-5′), 32.6 (C-3), 29.7, 29.1 (C-2′, C-4′), 23.1 (C-3′), 20.80, 20.75 (2C), 20.73 (4 × $COCH_3$); HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{38}H_{48}NO_{16}$ 774.2968, found 774.2969; *m/z* $[M + NH_4]^+$ calcd for $C_{38}H_{51}N_2O_{16}$ 791.3233, found 791.3237; *m/z* $[M + Na]^+$ calcd for $C_{38}H_{47}NNaO_{16}$ 796.2787, found 796.2788. Analytical data for glycal **16**: $[\alpha]_D^{20}$ = +33 (*c* 2.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93−7.89 (m, 2H, C*H*-Ar), 7.00−6.95 (m, 2H, C*H*-Ar), 6.05 (t, $J_{3,4} \approx J_{3,5} \approx$ 2.0 Hz, 1H, H-3), 5.76 (ddd, $J_{4,5}$ = 4.5 Hz, $J_{3,4}$ = 2.2 Hz, $J_{4,6}$ = 1.3 Hz, 1H, H-4), 5.51 (ddd, $J_{4,5}$ = 4.5 Hz, $J_{3,5}$ = 1.7 Hz, $J_{5,6}$ = 1.1 Hz, 1H, H-5), 5.45 (d, *J* = 16.0 Hz, 1H, C*H*HPhen), 5.39 (d, *J* = 16.0 Hz, 1H, CH*H*Phen), 5.29 (ddd, $J_{6,7}$ = 9.7 Hz, $J_{7,8b}$ = 3.9 Hz, $J_{7,8a}$ = 2.5 Hz, 1H, H-7), 4.63 (dd, $J_{8a,8b}$ = 12.4 Hz, $J_{7,8a}$ = 2.5 Hz, 1H, H-8a), 4.41 (dt, $J_{6,7}$ = 9.7 Hz, $J_{5,6} \approx J_{4,6} \approx$ 1.1 Hz, 1H, H-6), 4.24 (dd, $J_{8a,8b}$ = 12.4 Hz, $J_{7,8b}$ = 3.9 Hz, 1H, H-8b), 2.11, 2.09, 2.05, 2.04 (all s, 12H, 4 × COCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.8 (COPhen), 170.7, 170.5, 170.2, 169.6 (4 × $COCH_3$), 164.4 (C-Ar), 160.6 (C-1), 144.3 (C-2), 130.3 (2 × CH-Ar), 128.7 (C-Ar), 114.3 (2 × CH-Ar), 108.8 (C-3), 73.6 (C-6), 67.5 (C-7), 66.6 (CH_2Phen), 64.9 (C-4), 62.0 (C-8), 60.9 (C-5), 55.7 (OCH_3), 20.9, 20.8, 20.74, 20.70 (4 × $COCH_3$); HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{25}H_{28}NaO_{13}$ 559.1422, found 559.1445.

*Benzyl [2-(5-Amino-N-[(benzyloxy)carbonyl]-1-pentyl) 4,5,7,8-tetra-O-acetyl-3-deoxy-α,β-D-manno-oct-2-ulopyranosid]onate (**17β** and **17α**) and Benzyl 4,5,7,8-Tetra-O-acetyl-2,6-anhydro-3-deoxy-D-manno-oct-2-enosonate (**18**).* Thioglycoside **3** (1.14 g, 2.10 mmol, 1.0 equiv, β/α 7:1) and acceptor **9** (998 mg, 4.21 mmol, 2.0 equiv) were reacted according to the general procedure for glycosylation with thioglycoside donors and gave **17β** (1.21 g, 81%) and **17α** (192 mg, 13%), both as yellow oils (β/α 6.3:1.0). The physical and analytical data of **17β** and **17α** were in agreement with those published in the literature.[10] Analytical data for glycal **18**: $[\alpha]_D^{20}$ = +1.3 (*c* 1.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.34 (m, 5H, C*H*-Ar), 5.92 (t, $J_{3,4} \approx J_{3,5} \approx$ 2.0 Hz, 1H, H-3), 5.73−5.70 (m, 1H, H-4), 5.49−5.46 (m, 1H, H-5), 5.30−5.24 (m, 3H, H-7, CH_2Ph), 4.63 (dd, $J_{8a,8b}$ = 12.3 Hz, $J_{7,8a}$ = 2.3 Hz, 1H, H-8a), 4.36 (br d, $J_{6,7}$ = 9.7 Hz, 1H, H-6), 4.24 (dd, $J_{8a,8b}$ = 12.3 Hz, $J_{7,8b}$ = 4.0 Hz, 1H, H-8b), 2.09 (s, 6H, 2 × COCH_3), 2.04, 2.03 (all s, 6H, 2 × COCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 170.5, 170.2, 169.6 (4 × $COCH_3$), 160.9 (C-1), 144.7 (C-2), 135.3 (C-Ar), 128.8, 128.7, 128.5 (5 × CH-Ar), 107.9 (C-3), 73.4 (C-6), 67.39 (C-7), 67.37 (CH_2Ph), 64.8 (C-4), 62.0 (C-8), 60.8 (C-5), 20.9, 20.8, 20.75, 20.68 (4 × $COCH_3$); HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{23}H_{26}NaO_{11}$ 501.1367, found 501.1380.

*3′-Methoxyphenacyl [2-[5-Amino-N-[(benzyloxy)carbonyl]-1-pentyl] 4,5,7,8-tetra-O-acetyl-3-deoxy-α,β-D-manno-oct-2-ulopyranosid]onate (**19**).* Thioglycoside **6** (45 mg, 75 μmol, 1.0 equiv, β/α 7:1) and acceptor **9** (31 mg, 110 μmol, 1.5 equiv) were reacted according to the general procedure for glycosylation with thioglycoside donors and gave **19** (42 mg, 73%, β/α 6.6:1.0) as a yellow oil: $[\alpha]_D^{20}$ = +31 (*c* 5.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, β-anomer) δ 7.49−7.29 (m, 8H, C*H*-Ar), 7.19−7.14 (m, 1H, C*H*-Ar), 5.49 (d, *J* = 16.2 Hz, 1H, C*H*HPhen), 5.42 (d, *J* = 16.2 Hz, 1H, CH*H*Phen), 5.41−5.39 (m, 1H, H-5), 5.31 (ddd, $J_{3ax,4}$ = 13.0 Hz, $J_{3eq,4}$ = 4.6 Hz, $J_{4,5}$ = 3.1 Hz, 1H, H-4), 5.22 (ddd, $J_{6,7}$ = 9.5 Hz, $J_{7,8b}$ = 4.8 Hz, $J_{7,8a}$ = 2.4 Hz, 1H, H-7), 5.15−5.05 (m, 3H, CH_2Ph, N*H*Cbz), 4.42−4.30 (m, 3H, H-8a, H-8b, H-6), 3.88−3.79 (m, 1H, H-1a′), 3.86 (s, 3H, OCH_3), 3.56−3.48 (m, 1H, H-1b′), 3.24−3.17 (m, 2H, H-5ab′), 2.53 (dd, $J_{3ax,3eq}$ = 12.5 Hz, $J_{3eq,4}$ = 4.6 Hz, 1H, H-3eq), 2.17 (t, $J_{3ax,3eq} \approx J_{3ax,4} \approx$ 12.5 Hz, 1H, H-3ax), 2.12, 2.03, 2.00 (all s, 12H, 4 × COCH_3), 1.67−1.50, 1.47−1.38 (all m, 6H, H-2′, H-3′, H-4′); ^{13}C NMR (100 MHz, $CDCl_3$, β-anomer) δ 190.7 (COPhen), 170.9, 170.6, 170.0, 169.9 (4 × $COCH_3$), 167.5 (C-1), 160.1, 136.8, 135.1 (3 × C-Ar), 130.1, 128.6, 128.1, 120.9, 120.3, 112.1 (CH-Ar), 99.5 (C-2), 70.9 (C-6), 68.2 (C-7), 67.3 (C-4), 67.1 (CH_2Phen), 66.6 (CH_2Ph), 64.5 (C-1′), 64.3 (C-5), 62.8 (C-8), 55.6 (OCH_3), 41.0 (C-5′), 32.7 (C-3), 29.8, 29.2, 23.1 (C-2′, C-3′, C-4′), 20.9−20.8 (4 × $COCH_3$); HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{38}H_{48}NO_{16}$ 774.2968, found 774.2973; *m/z* $[M + Na]^+$ calcd for $C_{38}H_{47}NNaO_{16}$ 796.2787, found 796.2792; *m/z* $[2 M + Na]^+$ calcd for $C_{76}H_{94}N_2NaO_{32}$ 1569.5682, found 1569.5688.

*2′-Methoxyphenacyl [2-(5-Amino-N-(benzyloxycarbonyl)-1-pentyl) 4,5,7,8-tetra-O-acetyl-3-deoxy-α,β-D-manno-oct-2-ulopyranosid]onate (**20**).* Thioglycoside **7** (45 mg, 75 μmol, 1.0 equiv, β/α 7:1) and acceptor **9** (31 mg, 110 μmol, 1.5 equiv) were reacted according to the general procedure for glycosylation with thioglycoside donors and gave **20** (47 mg, 80%, β/α 4.6:1.0) as a colorless oil: $[\alpha]_D^{20}$ = +31 (*c* 4.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, β-anomer) δ 8.00−7.97 (m, 1H, C*H*-Ar), 7.58−7.52 (m, 1H, C*H*-Ar), 7.37−7.29 (m, 5H, C*H*-Ar), 7.06−6.99 (m, 2H, C*H*-Ar), 5.40−5.38 (m, 1H, H-5), 5.36−5.33 (m, 2H, CH_2Phen), 5.32 (ddd, $J_{3ax,4}$ = 12.5 Hz, $J_{3eq,4}$ = 5.3 Hz, $J_{4,5}$ = 3.1 Hz, 1H, H-4), 5.22 (ddd, $J_{6,7}$ = 9.5 Hz, $J_{7,8b}$ = 5.0 Hz, $J_{7,8a}$ = 2.2 Hz, 1H, H-7), 5.10−5.07 (m, 2H, CH_2Ph), 4.41 (dd, $J_{8a,8b}$ = 12.3 Hz, $J_{7,8a}$ = 2.1 Hz, 1H, H-8a), 4.37 (dd, $J_{6,7}$ = 9.6 Hz, $J_{5,6}$ = 1.1 Hz, 1H, H-6), 4.32 (dd, $J_{8a,8b}$ = 12.3 Hz, $J_{7,8b}$ = 5.1 Hz, 1H, H-8b), 3.97 (s, 3H, OCH_3), 3.86−3.80 (m, 1H, H-1a′), 3.59−3.52 (m, 1H, H-1b′), 3.25−3.17 (m, 2H, H-5ab′), 2.52 (dd, $J_{3ax,3eq}$ = 12.5 Hz, $J_{3eq,4}$ = 4.8 Hz, 1H, H-3eq), 2.15 (t, $J_{3ax,3eq} \approx J_{3ax,4} \approx$ 12.5 Hz, 1H, H-3ax), 2.11, 2.02, 2.00 (all s, 12H, 4 × COCH_3), 1.68−1.50, 1.47−1.37 (all m, 6H, H-2′, H-3′, H-4′); ^{13}C NMR (100 MHz, $CDCl_3$, β-anomer) δ 191.3 (COPhen), 171.0, 170.7, 170.1, 169.9 (4 × $COCH_3$), 167.7 (C-1), 159.7, 135.4, 123.8 (3 × C-Ar), 135.4, 131.4, 128.6, 128.2, 128.1, 121.3, 111.7 (CH-Ar), 99.6 (C-2), 71.0 (CH_2Phen), 70.8 (C-6), 68.3 (C-7), 67.3 (C-4), 66.6 (CH_2Ph), 64.6 (C-1′), 64.4 (C-5), 62.9 (C-8), 55.7 (OCH_3), 41.1 (C-5′), 32.8 (C-3), 29.8, 29.2, 23.2 (C-2′, C-3′, C-4′), 20.9−20.8 (4 × $COCH_3$); HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{38}H_{48}NO_{16}$ 774.2968, found 774.2985; *m/z* $[M + Na]^+$ calcd for $C_{38}H_{47}NNaO_{16}$ 796.2787, found 796.2804; *m/z* $[2 M + Na]^+$ calcd for $C_{76}H_{94}N_2NaO_{32}$ 1569.5682, found 1569.5711.

*Phenacyl [2-[5-Amino-N-[(benzyloxy)carbonyl]-1-pentyl] 4,5,7,8-tetra-O-acetyl-3-deoxy-α,β-D-manno-oct-2-ulopyranosid]onate (**21**).* Thioglycoside **8** (45 mg, 75 μmol, 1.0 equiv, β/α 7:1) and acceptor **9** (31 mg, 110 μmol, 1.5 equiv) were reacted according to the general procedure for glycosylation with thioglycoside donors and gave **21** (45 mg, 77%, β/α 6.2:1.0) as a colorless oil: $[\alpha]_D^{20}$ = +36 (*c* 4.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, β-anomer) δ 7.94−7.89 (m, 2H, C*H*-Ar), 7.66−7.60 (m, 1H, C*H*-Ar), 7.53−7.47 (m, 2H, C*H*-Ar), 7.38−7.29 (m, 5H, C*H*-Ar), 5.50 (d, *J* = 16.2 Hz, 1H, C*H*HPhen), 5.43 (d, *J* = 16.2 Hz, 1H, CH*H*Phen), 5.41−5.38 (m, 1H, H-5), 5.32 (ddd, $J_{3ax,4}$ = 13.0 Hz, $J_{3eq,4}$ = 4.6 Hz, $J_{4,5}$ = 3.0 Hz, 1H, H-4), 5.22 (ddd, $J_{6,7}$ = 9.6 Hz, $J_{7,8b}$ = 4.9 Hz, $J_{7,8a}$ = 2.3 Hz, 1H, H-7), 5.11−5.06 (m, 2H, CH_2Ph), 5.03 (t, *J* = 5.8 Hz, 1H, N*H*Cbz), 4.42−4.31 (m, 3H, H-8a, H-8b, H-6), 3.86−3.79 (m, 1H, H-1a′), 3.55−3.49 (m, 1H, H-1b′), 3.25−3.17 (m, 2H, H-5ab′), 2.53 (dd, $J_{3ax,3eq}$ = 12.5 Hz, $J_{3eq,4}$ = 4.7 Hz, 1H, H-3eq), 2.17 (t, $J_{3ax,3eq} \approx J_{3ax,4} \approx$ 12.5 Hz, 1H, H-3ax), 2.11, 2.03, 2.00, 1.99 (all s, 12H, 4 × COCH_3), 1.67−1.51, 1.47−1.38 (all m, 6H, H-2′, H-3′, H-4′); ^{13}C NMR (100 MHz, $CDCl_3$, β-anomer) δ 190.9 (COPhen), 171.0, 170.6, 170.0, 169.9 (4 × $COCH_3$), 167.6 (C-1), 136.8, 133.8 (2 × C-Ar), 134.3,

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129.1, 128.6, 128.2, 128.0 (CH-Ar), 99.6 (C-2), 70.9 (C-6), 68.2 (C-7), 67.3 (C-4), 67.0 (CH_2Phen), 66.7 (CH_2Ph), 64.6 (C-1′), 64.4 (C-5), 62.8 (C-8), 41.1 (C-5′), 32.8 (C-3), 29.7, 29.2, 23.2 (C-2′, C-3′, C-4′), 20.92−20.85 (4 × $COCH_3$); HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{37}H_{46}NO_{15}$ 744.2862, found 744.2878; m/z [M + Na]$^+$ calcd for $C_{37}H_{45}NNaO_{15}$ 766.2681, found 766.2699; m/z [2 M + Na]$^+$ calcd for $C_{74}H_{90}N_2NaO_{30}$ 1509.5471, found 1509.5505.

*4′-Methoxyphenacyl [2-(1-Nonyl) 4,5,7,8-tetra-O-acetyl-3-deoxy-α,β-D-manno-oct-2-ulopyranosid]onate (**22**).* Thioglycoside **2** (50 mg, 84 μmol, 1.0 equiv, β/α 7:1) and 1-nonanol (**10**, 22 μL, 130 μmol, 1.5 equiv) were reacted according to the general procedure for glycosylation with thioglycoside donors and gave **22** (37 mg, 65%, β/α 5.3:1.0) as a yellow oil: $[\alpha]_D^{20}$ = +48 (*c* 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, β-anomer) δ 7.92−7.88 (m, 2H, C*H*-Ar), 6.99−6.95 (m, 2H, C*H*-Ar), 5.47 (d, *J* = 15.8 Hz, 1H, C*H*HPhen), 5.42−5.39 (m, 1H, H-5), 5.36 (d, *J* = 15.8 Hz, 1H, CH*H*Phen), 5.35 (ddd, $J_{3ax,4}$ = 13.0 Hz, $J_{3eq,4}$ = 4.6 Hz, $J_{4,5}$ = 3.1 Hz, 1H, H-4), 5.22 (ddd, $J_{7,8a}$ = 9.6 Hz, $J_{7,8b}$ = 4.3 Hz, $J_{6,7}$ = 3.1 Hz, 1H, H-7), 4.41−4.35 (m, 3H, H-8a, H-8b, H-6), 3.89 (s, 3H, OCH_3), 3.81 (dt, *J* = 9.0, 6.5 Hz, 1H, H-1a′), 3.48 (dt, *J* = 9.0, 6.8 Hz, 1H, H-1b′), 2.54 (ddd, $J_{3eq,3ax}$ = 12.5 Hz, $J_{3eq,4}$ = 4.8 Hz, $J_{3,5}$ = 0.8 Hz, 1H, H-3eq), 2.17 (t, $J_{3eq,3ax} \approx J_{3ax,4} \approx$ 12.7 Hz, 1H, H-3ax), 2.12, 2.02, 2.00 (all s, 12H, 4 × $COCH_3$), 1.64−1.56 (m, 2H, H-2′), 1.36−1.24 (m, 12H, H-3′, H-4′, H-5′, H-6′, H-7′, H-8′), 0.88 (t, *J* = 6.8 Hz, 3H, H-9′); ^{13}C NMR (100 MHz, $CDCl_3$, β-anomer) δ 189.1 (COPhen), 170.9, 170.6, 170.0, 169.9 (4 × $COCH_3$), 167.7 (C-1, $^3J_{C1,H3ax}$ = 5.2 Hz), 164.4 (C-Ar), 130.2 (2 × CH-Ar), 126.9 (C-Ar), 114.3 (2 × CH-Ar), 99.6 (C-2), 70.9 (C-6), 68.3 (C-7), 67.4 (C-4), 66.7 (CH_2Phen), 65.0 (C-1′), 64.5 (C-5), 62.8 (C-8), 55.7 (OCH_3), 32.8 (C-3), 32.0, 29.8, 29.6, 29.5, 29.4, 26.0, 22.8 (C-2′, C-3′, C-4′, C-5′, C-6′, C-7′, C-8′), 20.91, 20.86 (2C), 20.83 (4 × $COCH_3$), 14.2 (C-9′); HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{34}H_{49}O_{14}$ 681.3117, found 681.3091; m/z [M + Na]$^+$ calcd for $C_{34}H_{48}NaO_{14}$ 703.2936, found 703.2913; m/z [2 M + Na]$^+$ calcd for $C_{68}H_{96}NaO_{28}$ 1385.5980, found 1386.5926.

*Benzyl [2-(1-Nonyl) 4,5,7,8-tetra-O-acetyl-3-deoxy-α,β-D-manno-oct-2-ulopyranosid]onate (**23**).* Thioglycoside **3** (50 mg, 93 μmol, 1.0 equiv, β/α 7:1) and 1-nonanol (**10**, 24 μL, 140 μmol, 1.5 equiv) were reacted according to the general procedure for glycosylation with thioglycoside donors and gave **23** (37 mg, 87%, β/α 3.5:1.0) as a yellow oil: $[\alpha]_D^{20}$ = +42 (*c* 5.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, β-anomer) δ 7.39−7.34 (m, 5H, C*H*-Ar), 5.28−5.16 (m, 4H, H-5, H-7, CH_2Ph), 4.87 (ddd, $J_{3ax,4}$ = 13.2 Hz, $J_{3eq,4}$ = 4.6 Hz, $J_{4,5}$ = 3.0 Hz, 1H, H-4), 4.35−4.33 (m, 2H, H-8a, H-8b), 4.20 (dd, $J_{6,7}$ = 9.6 Hz, $J_{5,6}$ = 1.4 Hz, 1H, H-6), 3.70 (dt, *J* = 9.1, 6.6 Hz, 1H, C*H*H), 3.17 (dt, *J* = 9.1, 6.8 Hz, 1H, CH*H*), 2.40 (dd, $J_{3eq,3ax}$ = 12.5 Hz, $J_{3eq,4}$ = 4.5 Hz, 1H, H-3eq), 2.10 (t, $J_{3eq,3ax} \approx J_{3ax,4} \approx$ 12.5 Hz, 1H, H-3ax), 2.10, 2.09, 2.00, 1.98 (all s, 12H, 4 × $COCH_3$), 1.51−1.44 (m, 2H, CH_2), 1.33−1.19 (m, 12H, 6 × CH_2), 0.88 (t, *J* = 6.8 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$, β-anomer) δ 170.9, 170.7, 170.0, 169.9 (4 × $COCH_3$), 168.0 (C-1, $^3J_{C1,H3ax}$ = 6.4 Hz), 135.1 (C-Ar), 128.9−128.5 (CH-Ar), 99.6 (C-2), 70.8 (C-6), 68.2 (C-7), 67.8 (CH_2Ph), 67.5 (C-4), 65.0 (CH_2), 64.3 (C-5), 62.7 (C-8), 32.7 (C-3), 32.0, 29.68, 29.65, 29.5, 29.4, 26.0, 22.8 (7 × CH_2), 20.92, 20.86, 20.84, 20.82 (4 × $COCH_3$), 14.3 (CH_3); HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{32}H_{46}NaO_{12}$ 645.2881, found 645.2887; m/z [2 M + Na]$^+$ calcd for $C_{64}H_{92}NaO_{24}$ 1267.5871, found 1267.5890.

*4′-Methoxyphenacyl (2-Cyclohexyl 4,5,7,8-tetra-O-acetyl-3-deoxy-α,β-D-manno-oct-2-ulopyranosid)onate (**24**).* Thioglycoside **2** (50 mg, 84 μmol, 1.0 equiv, β/α 7:1) and cyclohexanol (**11**, 13 μL, 130 μmol, 1.5 equiv) were reacted according to the general procedure for glycosylation with thioglycoside donors and gave **24** (40 mg, 76%, β/α 4.0:1.0) as a yellow oil: $[\alpha]_D^{20}$ = +43 (*c* 4.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, β-anomer) δ 7.92−7.88 (m, 2H, C*H*-Ar), 6.99−6.94 (m, 2H, CH-Ar), 5.47 (d, *J* = 15.9 Hz, 1H, C*H*HPhen), 5.41−5.40 (m, 1H, H-5), 5.36 (ddd, $J_{3ax,4}$ = 12.9 Hz, $J_{3eq,4}$ = 4.7 Hz, $J_{4,5}$ = 3.2 Hz, 1H, H-4), 5.33 (d, *J* = 15.8 Hz, 1H, CH*H*Phen), 5.19 (ddd, $J_{6,7}$ = 9.6 Hz, $J_{7,8b}$ = 4.9 Hz, $J_{7,8a}$ = 2.3 Hz, 1H, H-7), 4.40 (dd, $J_{8a,8b}$ = 12.1 Hz, $J_{7,8a}$ = 2.3 Hz, 1H, H-8a), 4.38 (dd, $J_{6,7}$ = 9.6 Hz, $J_{5,6}$ = 1.4 Hz, 1H, H-6), 4.33 (dd, $J_{8a,8b}$ = 12.3 Hz, $J_{7,8b}$ = 4.9 Hz, 1H, H-8b), 3.89−3.83 (m, 1H, CH_{Cy}), 3.88 (s, 3H, OCH_3), 2.53 (ddd, $J_{3ax,3eq}$ = 12.4 Hz, $J_{3eq,4}$ = 4.7 Hz, $J_{3eq,5}$ = 0.7 Hz, 1H, H-3eq), 2.16 (t, $J_{3ax,3eq} \approx J_{3ax,4} \approx$ 12.4 Hz, 1H, H-3ax), 2.11, 2.02, 1.999, 1.994 (all s, 12H, 4 × $COCH_3$), 1.95−1.14 (m, 10H, 5 × CH_{2Cy}); ^{13}C NMR (100 MHz, $CDCl_3$, β-anomer) δ 189.2 (COPhen), 170.8, 170.6, 170.1, 169.8 (4 × $COCH_3$), 168.2 (C-1, $^3J_{C1,H3ax}$ = 5.2 Hz), 164.4 (C-Ar), 130.2 (2 × CH-Ar), 126.9 (C-Ar), 114.3 (2 × CH-Ar), 99.8 (C-2), 74.5 (CH_{Cy}), 70.8 (C-6), 68.4 (C-7), 67.4 (C-4), 66.7 (CH_2Phen), 64.5 (C-5), 62.8 (C-8), 55.6 (OCH_3), 34.8, 33.6 (2 × CH_{2Cy}), 33.1 (C-3), 25.5, 24.5, 24.4 (3 × CH_{2Cy}), 20.90, 20.85 (2C), 20.82 (4 × $COCH_3$); HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{31}H_{40}NaO_{14}$ 659.2310, found 659.2315; m/z [2 M + Na]$^+$ calcd for $C_{62}H_{80}NaO_{28}$ 1295.4728, found 1295.4732.

*Benzyl (2-Cyclohexyl 4,5,7,8-tetra-O-acetyl-3-deoxy-α,β-D-manno-oct-2-ulopyranosid)onate (**25**).* Thioglycoside **3** (50 mg, 93 μmol, 1.0 equiv, β/α 7:1) and cyclohexanol (**11**, 15 μL, 140 μmol, 1.5 equiv) were reacted according to the general procedure for glycosylation with thioglycoside donors and gave **25** (43 mg, 80%, β/α 2.2:1.0) as a yellow oil: $[\alpha]_D^{20}$ = +69 (*c* 0.69, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, β-anomer) δ 7.41−7.33 (m, 5H, C*H*-Ar), 5.27−5.25 (m, 1H, H-5), 5.26 (d, *J* = 12.0 Hz, 1H, C*H*HPh), 5.18 (d, *J* = 12.0 Hz, 1H, CH*H*Ph), 5.16 (ddd, $J_{6,7}$ = 9.5 Hz, $J_{7,8b}$ = 4.6 Hz, $J_{7,8a}$ = 2.3 Hz, 1H, H-7), 4.85 (ddd, $J_{3ax,4}$ = 13.2 Hz, $J_{3eq,4}$ = 4.6 Hz, $J_{4,5}$ = 3.0 Hz, 1H, H-4), 4.37 (dd, $J_{8a,8b}$ = 12.3 Hz, $J_{7,8a}$ = 2.4 Hz, 1H, H-8a), 4.31 (dd, $J_{8a,8b}$ = 12.3 Hz, $J_{7,8b}$ = 4.7 Hz, 1H, H-8b), 4.15 (dd, $J_{6,7}$ = 9.5 Hz, $J_{5,6}$ = 1.4 Hz, 1H, H-6), 3.66−3.58 (m, 1H, CH_{Cy}), 2.40 (ddd, $J_{3ax,3eq}$ = 12.5 Hz, $J_{3eq,4}$ = 4.6 Hz, $J_{3eq,5}$ = 0.8 Hz, 1H, H-3eq), 2.09 (t, $J_{3ax,3eq} \approx J_{3ax,4} \approx$ 12.3 Hz, 1H, H-3ax), 2.09, 2.06, 2.00, 1.97 (all s, 12H, 4 × $COCH_3$), 1.94−1.00 (m, 10H, 5 × CH_{2Cy}); ^{13}C NMR (100 MHz, $CDCl_3$, β-anomer) δ 170.7, 170.6, 169.94, 169.91 (4 × $COCH_3$), 168.3 (C-1, $^3J_{C1,H3ax}$ = 6.2 Hz), 134.9, (C-Ar), 128.7−128.3 (CH-Ar), 99.8 (C-2), 74.6 (CH_{Cy}), 70.7 (C-6), 68.3 (C-7), 67.7 (CH_2Ph), 67.2 (C-4), 64.2 (C-5), 62.6 (C-8), 34.8 (CH_{2Cy}), 33.3 (CH_{2Cy}), 33.0 (C-3), 25.4, 24.4, 24.3 (3 × CH_{2Cy}), 20.88, 20.82, 20.79, 20.77 (4 × $COCH_3$); HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{29}H_{38}NaO_{12}$ 601.2255, found 601.2246; m/z [2 M + Na]$^+$ calcd for $C_{58}H_{76}NaO_{24}$ 1179.4619, found 1179.4595.

*4′-Methoxyphenacyl [2-(2′-Adamantyl) 4,5,7,8-tetra-O-acetyl-3-deoxy-α,β-D-manno-oct-2-ulopyranosid]onate (**26**).* Thioglycoside **2** (50 mg, 84 μmol, 1.0 equiv, β/α 7:1) and 2-adamantanol (**12**, 19 mg, 130 μmol, 1.5 equiv) were reacted according to the general procedure for glycosylation with thioglycoside donors and gave **26** (34 mg, 58%, β/α 4.3:1.0) as a colorless oil: $[\alpha]_D^{20}$ = +7 (*c* 2.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, β-anomer) δ 7.93−7.88 (m, 2H, C*H*-Ar), 6.99−6.94 (m, 2H, C*H*-Ar), 5.46 (d, *J* = 15.9 Hz, 1H, C*H*HPhen), 5.43−5.35 (m, 2H, H-4, H-5), 5.33 (d, *J* = 15.9 Hz, 1H, CH*H*Phen), 5.17 (ddd, $J_{6,7}$ = 9.5 Hz, $J_{7,8b}$ = 4.8 Hz, $J_{7,8a}$ = 2.2 Hz, 1H, H-7), 4.39−4.34 (m, 2H, H-8a, H-6), 4.29 (dd, $J_{8a,8b}$ = 12.2 Hz, $J_{7,8b}$ = 5.0 Hz, 1H, H-8b), 4.08−4.04 (m, 1H, C*H*-Ad), 3.89 (s, 3H, OCH_3), 2.55 (ddd, $J_{3ax,3eq}$ = 12.0 Hz, $J_{3eq,4}$ = 4.7 Hz, $J_{3eq,5}$ = 0.9 Hz, 1H, H-3eq), 2.20 (t, $J_{3ax,3eq} \approx J_{3ax,4} \approx$ 12.0 Hz, 1H, H-3ax), 2.16−2.06 (m, 2H, CH_2-Ad), 2.12, 2.02, 2.00 (all s, 12H, 4 × $COCH_3$), 2.06−2.01 (m, 1H, C*H*-Ad), 1.85−1.68 (m, 9H, 3 × CH_2-Ad, 3 × C*H*-Ad), 1.55−1.45 (m, 2H, CH_2-Ad); ^{13}C NMR (100 MHz, $CDCl_3$, β-anomer) δ 189.3 (COPhen), 170.8, 170.6, 170.1, 169.8 (4 × $COCH_3$), 168.2 (C-1, $^3J_{C1,H3ax}$ = 5.2 Hz), 164.3 (C-Ar), 130.2 (2 × CH-Ar), 127.0 (C-Ar), 114.3 (2 × CH-Ar), 99.8 (C-2), 78.2 (CH-Ad), 70.7 (C-6), 68.4 (C-7), 67.5 (C-4), 66.6 (CH_2Phen), 64.5 (C-5), 62.8 (C-8), 55.7 (OCH_3), 37.7, 37.0, 36.8 (3 × CH_2-Ad), 34.4, 33.5 (2 × CH-Ad), 33.2 (C-3), 31.69, 31.67 (2 × CH_2-Ad), 27.4, 27.1 (2 × CH-Ad), 20.92, 20.88 (2C), 20.85 (4 × $COCH_3$); HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{35}H_{44}NaO_{14}$ 711.2623, found 711.2604; m/z [2 M + Na]$^+$ calcd for $C_{70}H_{88}NaO_{28}$ 1399.5354, found 1399.5309.

*Benzyl [2-(2′-Adamantyl) 4,5,7,8-tetra-O-acetyl-3-deoxy-α,β-D-manno-oct-2-ulopyranosid]onate (**27**).* Thioglycoside **3** (40 mg, 74 μmol, 1.0 equiv, β/α 7:1) and 2-adamantanol (**12**, 16 mg, 110 μmol, 1.5 equiv) were reacted according to the general procedure for glycosylation with thioglycoside donors and gave **27** (35 mg, 74%, β/α 2.4:1.0) as a yellow oil: $[\alpha]_D^{20}$ = +54 (*c* 3.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, β-anomer) δ 7.40−7.33 (m, 5H, C*H*-Ar), 5.27−5.25 (m, 1H, H-5), 5.24 (d, *J* = 12.1 Hz, 1H, C*H*HPh), 5.16 (d, *J* = 12.2 Hz, 1H, C*H*HPh), 5.14 (ddd, $J_{6,7}$ = 9.5 Hz, $J_{7,8b}$ = 4.7 Hz, $J_{7,8a}$ = 2.3 Hz, 1H, H-7), 4.87 (ddd, $J_{3ax,4}$ = 13.2 Hz, $J_{3eq,4}$ = 4.6 Hz, $J_{4,5}$ = 3.0 Hz, 1H, H-4), 4.34 (dd, $J_{8a,8b}$ = 12.2 Hz, $J_{7,8a}$ = 2.2 Hz, 1H, H-8a), 4.27 (dd, $J_{8a,8b}$ = 12.2 Hz, $J_{7,8b}$ = 4.8 Hz, 1H, H-8b), 4.13 (dd, $J_{6,7}$ = 9.5 Hz, $J_{5,6}$ = 1.4 Hz, 1H, H-6), 3.86−3.82 (m, 1H, C*H*-Ad), 2.43 (dd, $J_{3ax,3eq}$ = 12.5 Hz, $J_{3eq,4}$ = 4.6 Hz, 1H, H-3eq), 2.13 (t,

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$J_{3ax,3eq} \approx J_{3ax,4} \approx$ 12.9 Hz, 1H, H-3ax), 2.10, 2.08, 2.00, 1.98 (all s, 12H, 4 × COCH_3), 2.11−1.96 (m, 2H, CH_2-Ad), 1.98−1.94 (m, 1H, C*H*-Ad), 1.79−1.68 (m, 3H, 2 × C*H*-Ad, C*H*HAd), 1.67−1.58 (m, 4H, 2 × CH_2-Ad), 1.51−1.33 (m, 4H, CH_2-Ad, C*H*-Ad, CH*H*-Ad); ^{13}C NMR (100 MHz, $CDCl_3$, *β*-anomer) *δ* 170.8, 170.7, 170.05, 169.98 (4 × $COCH_3$), 168.4 (C-1, $^3J_{C1,H3ax}$ = 6.3 Hz), 135.1 (C-Ar), 128.8−128.7 (*C*H-Ar), 99.8 (C-2), 78.2 (*C*H-Ad), 70.7 (C-6), 68.4 (C-7), 67.6 (CH_2Ph), 67.4 (C-4), 64.3 (C-5), 62.7 (C-8), 37.6, 36.9, 36.7 (3 × CH_2-Ad), 34.3, 33.3 (2 × CH-Ad), 33.1 (C-3), 31.7, 31.6 (2 × CH_2-Ad), 27.4, 27.0 (2 × CH-Ad), 20.93, 20.89, 20.86, 20.85 (4 × $COCH_3$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{33}H_{42}NaO_{12}$ 653.2568, found 653.2557; *m/z* [M + K]$^+$ calcd for $C_{33}H_{42}KO_{12}$ 669.2308, found 669.2295; *m/z* [2 M + Na]$^+$ calcd for $C_{66}H_{84}NaO_{24}$ 1283.5245, found 1283.5208.

*4′-Methoxyphenacyl [2-(1′-Adamantyl) 4,5,7,8-tetra-O-acetyl-3-deoxy-α,β-D-manno-oct-2-ulopyranosid]onate (**28**).* Thioglycoside **2** (50 mg, 84 *μ*mol, 1.0 equiv, *β*/*α* 7:1) and 1-adamantanol (**13**, 19 mg, 130 *μ*mol, 1.5 equiv) were reacted according to the general procedure for glycosylation with thioglycoside donors and gave **28** (23 mg, 40%, *β*/*α* 1.6:1.0) as a colorless oil: $[\alpha]_D^{20}$ = +34 (*c* 1.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, *β*-anomer) *δ* 7.94−7.89 (m, 2H, C*H*-Ar), 7.00−6.94 (m, 2H, C*H*-Ar), 5.49 (d, *J* = 15.8 Hz, 1H, C*H*HPhen), 5.40−5.37 (m, 1H, H-5), 5.33−5.18 (m, 3H, CH*H*Phen, H-4, H-7), 4.57 (dd, $J_{6,7}$ = 9.6 Hz, $J_{5,6}$ = 1.4 Hz, 1H, H-6), 4.48 (dd, $J_{8a,8b}$ = 12.2 Hz, $J_{7,8a}$ = 2.2 Hz, 1H, H-8a), 4.32 (dd, $J_{8a,8b}$ = 12.2 Hz, $J_{7,8b}$ = 5.2 Hz, 1H, H-8b), 3.89 (s, 3H, OCH_3), 2.51 (ddd, $J_{3ax,3eq}$ = 12.5 Hz, $J_{3eq,4}$ = 4.7 Hz, $J_{3eq,5}$ = 0.8 Hz, 1H, H-3eq), 2.21 (t, $J_{3ax,3eq} \approx J_{3ax,4} \approx$ 12.5 Hz, 1H, H-3ax), 2.15−2.10 (m, 3H, 3 × C*H*-Ad), 2.11, 2.026, 2.015, 1.99 (all s, 12H, 4 × COCH_3), 1.96−1.90 (m, 6H, 3 × CH_2-Ad), 1.66−1.58 (m, 6H, 3 × CH_2-Ad); ^{1}H NMR (400 MHz, $CDCl_3$, *α*-anomer) *δ* 7.94−7.89 (m, 2H, C*H*-Ar), 7.00−6.94 (m, 2H, C*H*-Ar), 5.53 (d, *J* = 15.8 Hz, 1H, C*H*HPhen), 5.42−5.36 (m, 2H, H-5, H-4), 5.33−5.18 (m, 2H, CH*H*Phen, H-7), 4.69 (dd, $J_{8a,8b}$ = 12.3 Hz, $J_{7,8a}$ = 2.7 Hz, 1H, H-8a), 4.39 (dd, $J_{6,7}$ = 9.4 Hz, $J_{5,6}$ = 1.5 Hz, 1H, H-6), 4.15 (dd, $J_{8a,8b}$ = 12.3 Hz, $J_{7,8b}$ = 3.8 Hz, 1H, H-8b), 3.89 (s, 3H, OCH_3), 2.32−2.23 (m, 2H, H-3eq, H-3ax), 2.15−2.10 (m, 3H, 3 × C*H*-Ad), 2.08, 2.07, 1.99, 1.98 (all s, 12H, 4 × COCH_3), 1.96−1.90 (m, 6H, 3 × CH_2-Ad), 1.66−1.58 (m, 6H, 3 × CH_2-Ad); ^{13}C NMR (100 MHz, $CDCl_3$, *β*-anomer) *δ* 189.5 (COPhen), 170.8, 170.7, 170.3, 170.1 (4 × $COCH_3$), 169.9 (C-1, $^3J_{C1,H3ax}$ = overlapping), 164.3 (C-Ar), 130.3 (2 × CH-Ar), 127.0 (C-Ar), 114.2 (2 × CH-Ar), 98.9 (C-2), 79.2 (C-Ad), 71.3 (C-6), 68.5 (C-7), 67.2 (C-4), 66.6 (CH_2Phen), 64.6 (C-5), 63.2 (C-8), 55.7 (OCH_3), 43.6 (2C), 42.9 (3 × CH_2-Ad), 36.3 (2C), 36.1 (3 × CH_2-Ad), 35.5 (C-3), 31.22 (2C), 31.17 (3 × CH-Ad), 21.0−20.8 (4 × $COCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$, *α*-anomer) *δ* 189.8 (COPhen), 170.7, 170.6, 170.2, 169.8 (4 × $COCH_3$), 169.5 (C-1, $^3J_{C1,H3ax}$ < 1.0 Hz), 164.3 (C-Ar), 130.3 (2 × CH-Ar), 127.3 (C-Ar), 114.3 (2 × CH-Ar), 97.9 (C-2); 78.2 (C-Ad), 68.9 (C-6), 68.6 (C-7), 66.8 (C-4), 66.4 (CH_2Phen), 65.0 (C-5), 61.9 (C-8), 55.7 (OCH_3), 43.6 (2C), 42.9 (3 × CH_2-Ad), 36.3 (2C), 36.1 (3 × CH_2Phen), 35.2 (C-3), 31.23 (2C), 31.17 (3 × CH-Ad), 21.0−20.8 (4 × $COCH_3$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{35}H_{44}NaO_{14}$ 711.2623, found 711.2604; *m/z* [2 M + Na]$^+$ calcd for $C_{70}H_{88}NaO_{28}$ 1399.5354, found 1399.5310.

*Benzyl [2-(1′-Adamantyl) 4,5,7,8-tetra-O-acetyl-3-deoxy-α,β-D-manno-oct-2-ulopyranosid]onate (**29**).* Thioglycoside **3** (50 mg, 93 *μ*mol, 1.0 equiv, *β*/*α* 7:1) and 1-adamantanol (**13**, 21 mg, 140 *μ*mol, 1.5 equiv) were reacted according to the general procedure for glycosylation with thioglycoside donors and gave **29** (30 mg, 51%, *β*/*α* 1.0:1.6) as a yellow oil: $[\alpha]_D^{20}$ = +43 (*c* 3.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, *β*-anomer) *δ* 7.44−7.32 (m, 5H, C*H*-Ar), 5.28−5.15 (m, 4H, H-5, H-7, CH_2Ph), 4.77 (ddd, $J_{3ax,4}$ = 13.4 Hz, $J_{3eq,4}$ = 4.5 Hz, $J_{4,5}$ = 2.9 Hz, 1H, H-4), 4.50 (dd, $J_{6,7}$ = 9.6 Hz, $J_{5,6}$ = 1.5 Hz, 1H, H-6), 4.46 (dd, $J_{8a,8b}$ = 12.3 Hz, $J_{7,8a}$ = 2.1 Hz, 1H, H-8a), 4.30 (dd, $J_{8a,8b}$ = 12.3 Hz, $J_{7,8b}$ = 5.2 Hz, 1H, H-8b), 2.31 (ddd, $J_{3ax,3eq}$ = 12.6 Hz, $J_{3eq,4}$ = 4.5 Hz, $J_{3eq,5}$ = 0.8 Hz, 1H, H-3eq), 2.12 (t, $J_{3ax,3eq} \approx J_{3ax,4} \approx$ 12.6 Hz, 1H, H-3ax), 2.10, 2.09, 2.01, 1.96 (all s, 12H, 4 × COCH_3), 2.05−1.97 (m, 3H, 3 × C*H*-Ad), 1.81−1.75 (m, 6H, 3 × CH_2-Ad), 1.57−1.42 (m, 6H, 3 × CH_2-Ad); ^{1}H NMR (400 MHz, $CDCl_3$, *α*-anomer) *δ* 7.44−7.32 (m, 5H, C*H*-Ar), 5.39−5.31 (m, 2H, H-5, H-4), 5.25−5.15 (m, 3H, CH_2Ph, H-7), 4.68 (dd, $J_{8a,8b}$ = 12.3 Hz, $J_{7,8a}$ = 2.7 Hz, 1H, H-8a), 4.34 (dd, $J_{6,7}$ = 9.5 Hz, $J_{5,6}$ = 1.5 Hz, 1H, H-6), 4.14 (dd, $J_{8a,8b}$ = 12.3 Hz, $J_{7,8b}$ = 3.8 Hz, 1H, H-8b), 2.19 (ddd, $J_{3ax,3eq}$ = 12.4 Hz, $J_{3eq,4}$ = 4.7 Hz, $J_{3eq,5}$ = 1.0 Hz, 1H, H-3eq), 2.06, 2.05, 1.98, 1.96 (all s, 12H, 4 × COCH_3), 2.05−1.97 (m, 3H, 3 × C*H*-Ad), 1.92 (t, $J_{3ax,3eq} \approx J_{3ax,4} \approx$ 12.4 Hz, 1H, H-3ax), 1.81−1.75 (m, 6H, 3 × CH_2-Ad), 1.57−1.42 (m, 6H, 3 × CH_2-Ad); ^{13}C NMR (100 MHz, $CDCl_3$, *β*-anomer) *δ* 170.8, 170.7, 170.1, 169.9 (4 × $COCH_3$), 169.8 (C-1, $^3J_{C1,H3ax}$ = overlapping), 134.9 (C-Ar), 129.0−128.8 (5 × CH-Ar), 98.7 (C-2), 79.0 (C-Ad), 71.3 (C-6), 68.4 (C-7), 67.7 (CH_2Ph), 66.9 (C-4), 64.4 (C-5), 63.2 (C-8), 43.5, 42.8 (2C, 3 × CH_2-Ad), 36.2, 36.0 (2C, 3 × CH_2-Ad), 35.3 (C-3), 31.1, 31.0 (2C, 3 × CH-Ad), 20.9−20.8 (4 × $COCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$, *α*-anomer) *δ* 170.59, 170.55, 170.51, 170.1 (4 × $COCH_3$), 169.4 (C-1, $^3J_{C1,H3ax}$ < 1.0 Hz), 134.8 (C-Ar), 129.0−128.8 (5 × CH-Ar), 97.6 (C-2), 78.1 (C-Ad), 68.8 (C-6), 68.6 (C-7), 67.6 (CH_2Ph), 66.8 (C-4), 65.0 (C-5), 61.9 (C-8), 43.5, 42.8 (2C, 3 × CH_2-Ad), 36.2, 36.0 (2C, 3 × CH_2-Ad), 35.0 (C-3), 31.1, 31.0 (2C, 3 × CH-Ad), 20.9−20.8 (4 × $COCH_3$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{33}H_{42}NaO_{12}$ 653.2568, found 653.2561; *m/z* [2 M + Na]$^+$ calcd for $C_{66}H_{84}NaO_{24}$ 1283.5245, found 1283.5226.

*4′-Methoxyphenacyl [(4,5,7,8-Tetra-O-acetyl-3-deoxy-α,β-D-manno-oct-2-ulopyranosyl)onate]-(2→6)-(Methyl 2,3-di-O-benzyl-α-D-glucopyranoside) (**30**).* Thioglycoside **2** (35 mg, 59 *μ*mol, 1.0 equiv, *β*/*α* 7:1) and methyl 2,3-di-*O*-benzyl-*α*-D-glucopyranoside (**14**, 30 mg, 80 *μ*mol, 1.4 equiv) were reacted according to the general procedure for glycosylation with thioglycoside donors and gave **30** (36 mg, 61%, *β*/*α* 5.0:1.0) as a yellow oil: $[\alpha]_D^{20}$ = +26 (*c* 1.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, *β*-anomer) *δ* 7.92−7.85 (m, 2H, C*H*-Ar), 7.43−7.26 (m, 10H, C*H*-Ar), 7.00−6.95 (m, 2H, C*H*-Ar), 5.44 (d, *J* = 15.8 Hz, 1H, C*H*HPhen), 5.37−5.35 (m, 1H, H-5), 5.36 (d, *J* = 15.8 Hz, 1H, CH*H*Phen), 5.25 (ddd, $J_{3ax,4}$ = 13.0 Hz, $J_{3eq,4}$ = 4.6 Hz, $J_{4,5}$ = 2.9 Hz, 1H, H-4), 5.20 (ddd, $J_{6,7}$ = 9.4 Hz, $J_{7,8b}$ = 5.1 Hz, $J_{7,8a}$ = 2.1 Hz, 1H, H-7), 4.97 (d, *J* = 11.1 Hz, 1H, C*H*HPh), 4.87 (d, *J* = 11.1 Hz, 1H, CH*H*Ph), 4.79 (d, *J* = 12.1 Hz, 1H, C*H*HPh), 4.67 (d, $J_{1,2}$ = 3.7 Hz, 1H, H-1Glc), 4.66 (d, *J* = 12.1 Hz, 1H, CH*H*Ph), 4.41 (dd, $J_{8a,8b}$ = 12.5 Hz, $J_{7,8a}$ = 2.3 Hz, 1H, H-8a), 4.37−4.29 (m, 2H, H-8b, H-6), 4.06 (dd, $J_{6a,6b}$ = 11.0 Hz, $J_{5,6a}$ = 2.1 Hz, 1H, H-6aGlc), 3.89 (s, 3H, OCH_3Phen), 3.87−3.80 (m, 2H, H-6bGlc, H-3Glc), 3.79−3.64 (m, 2H, H-5Glc, H-4Glc), 3.53 (dd, $J_{2,3}$ = 9.6 Hz, $J_{1,2}$ = 3.5 Hz, 1H, H-2Glc), 3.42 (s, 3H, OCH_3Glc), 2.50 (dd, $J_{3ax,3eq}$ = 12.6 Hz, $J_{3eq,4}$ = 4.8 Hz, 1H, H-3eq), 2.22 (t, $J_{3ax,3eq} \approx J_{3ax,4} \approx$ 12.6 Hz, 1H, H-3ax), 2.08, 2.02, 2.00, 1.99 (all s, 12H, 4 × COCH_3); ^{13}C NMR (100 MHz, $CDCl_3$, *β*-anomer) *δ* 189.6 (COPhen), 171.1, 170.6, 170.0, 169.9 (4 × $COCH_3$), 167.4 (C-1, $^3J_{C1,H3ax}$ = 5.6 Hz), 164.5 (C-Ar), 139.1, 138.4 (2 × C-Ar), 130.3−127.7 (*C*H-Ar), 126.7 (C-Ar), 114.3 (*C*H-Ar), 99.8 (C-2), 98.4 (C-1Glc), 81.9 (C-3Glc), 79.6 (C-2Glc), 75.8, 73.3 (2 × CH_2Ph), 71.1 (C-6), 70.4 (C-5Glc), 70.2 (C-4Glc), 68.2 (C-7), 67.3 (C-4), 66.8 (CH_2Phen), 64.3 (C-5), 63.7 (C-6Glc), 62.9 (C-8), 55.7 (OCH_3Phen), 55.3 (OCH_3Glc), 32.4 (C-3), 20.9 (2C), 20.81, 20.76 (4 × $COCH_3$); HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{46}H_{54}NaO_{19}$ 933.3152, found 933.3122; *m/z* [2 M + Na]$^+$ calcd for $C_{92}H_{108}NaO_{38}$ 1843.6411, found 1843.6353.

*Benzyl [(4,5,7,8-Tetra-O-acetyl-3-deoxy-α,β-D-manno-oct-2-ulopyranosyl)onate]-(2 → 6)-(Methyl 2,3-di-O-benzyl-α-D-glucopyranoside) (**31**).* Thioglycoside **3** (35 mg, 65 *μ*mol, 1.0 equiv, *β*/*α* 7:1) and methyl 2,3-di-*O*-benzyl-*α*-D-glucopyranoside (**14**, 33 mg, 88 *μ*mol, 1.4 equiv) were reacted according to the general procedure for glycosylation with thioglycoside donors and gave **31** (48 mg, 78%, *β*/*α* 3.7:1.0) as a yellow oil: $[\alpha]_D^{20}$ = +33 (*c* 3.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, *β*-anomer) *δ* 7.40−7.28 (m, 15H, C*H*-Ar), 5.26−5.24 (m, 1H, H-5), 5.21−5.19 (m, 2H, CH_2Ph), 5.15 (ddd, $J_{6,7}$ = 9.3 Hz, $J_{7,8b}$ = 4.7 Hz, $J_{7,8a}$ = 2.3 Hz, 1H, H-7), 4.97 (d, *J* = 11.2 Hz, 1H, C*H*HPh), 4.88 (ddd, $J_{3ax,4}$ = 13.1 Hz, $J_{3eq,4}$ = 4.6 Hz, $J_{4,5}$ = 2.9 Hz, 1H, H-4), 4.78 (d, *J* = 12.0 Hz, 1H, C*H*HPh), 4.77 (d, *J* = 11.2 Hz, 1H, CH*H*Ph), 4.65 (d, *J* = 12.2 Hz, 1H, CH*H*Ph), 4.61 (d, $J_{1,2}$ = 3.6 Hz, 1H, H-1Glc), 4.34 (dd, $J_{8a,8b}$ = 12.5 Hz, $J_{7,8a}$ = 2.4 Hz, 1H, H-8a), 4.29 (dd, $J_{8a,8b}$ = 12.4 Hz, $J_{7,8b}$ = 4.8 Hz, 1H, H-8b), 4.13 (dd, $J_{6,7}$ = 9.5 Hz, $J_{5,6}$ = 1.3 Hz, 1H, H-6), 3.99 (dd, $J_{6a,6b}$ = 11.0 Hz, $J_{5,6a}$ = 2.0 Hz, 1H, H-6aGlc), 3.78 (t, $J_{2,3} \approx J_{3,4} \approx$ 9.2 Hz, 1H, H-3Glc), 3.72−3.65 (m, 1H, H-5Glc), 3.59 (dd, $J_{6a,6b}$ = 11.0 Hz, $J_{5,6b}$ = 5.2 Hz, 1H, H-6bGlc), 3.53−3.44 (m, 2H, H-4Glc, H-2Glc), 3.38 (s, 3H, OCH_3), 2.40 (dd, $J_{3ax,3eq}$ = 12.5 Hz, $J_{3eq,4}$ = 4.6 Hz, 1H, H-3eq), 2.15 (t, $J_{3ax,3eq} \approx J_{3ax,4} \approx$ 12.5 Hz, 1H, H-3ax), 2.064, 2.062, 2.00, 1.98 (all s, 12H, 4 × COCH_3); ^{13}C NMR (100 MHz, $CDCl_3$, *β*-anomer) *δ* 171.1, 170.5, 169.90, 169.88 (4 × $COCH_3$), 167.6 (C-1, $^3J_{C1,H3ax}$ = 6.2 Hz), 139.0,

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138.2, 134.9 (3 × C-Ar), 128.9−127.8 (15 × CH-Ar), 99.8 (C-2), 98.2 (C-1Glc), 81.7 (C-3Glc), 79.7 (C-2Glc), 75.6, 73.3 (2 × CH_2Ph), 71.0 (C-6), 70.3, 70.2 (C-5Glc, C-4Glc), 68.1 (C-7), 67.9 (CH_2Ph), 67.1 (C-4), 64.08 (C-6Glc), 64.06 (C-5), 62.7 (C-8), 55.2 (OCH_3), 32.2 (C-3), 20.9, 20.82, 20.79, 20.7 (4 × $COCH_3$); HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{44}H_{52}NaO_{17}$ 875.3097, found 875.3117; m/z [2 M + Na]$^+$ calcd for $C_{88}H_{104}NaO_{34}$ 1727.6301, found 1727.6336.

*2-(1-Nonyl) (4,5,7,8-Tetra-O-acetyl-3-deoxy-β-D-manno-oct-2-ulopyranosid)onic Acid (**32**).* Kdo glycoside **22** (25 mg, 37 μmol, 1.0 equiv) was dissolved in 90% AcOH(aq) (1.1 mL), and the solution was heated to 35 °C. Freshly activated zinc powder (170 mg) was added in portions during 2 h. The mixture was filtered over Celite and rinsed with a 90% AcOH(aq) solution (5 mL) and a solution of EtOH/EtOAc (4 × 10 mL, 1:1 v/v). The solvents were concentrated under reduced pressure to afford a residue that was purified by silica gel flash chromatography (DCM/MeOH 1:0−8:2) to give carboxylic acid **32** (17 mg, 89%) as a white amorphous powder: $[\alpha]_D^{20}$ = +48 (c 1.8, MeOH); ^{1}H NMR (400 MHz, MeOD) δ 5.22 (br s, 1H, H-5), 5.17 (br t, J = 7.7 Hz, 1H, H-7), 5.00 (dt, $J_{3ax,4}$ = 12.6 Hz, $J_{3eq,4}$ = 3.6 Hz, 1H, H-4), 4.51 (d, $J_{8a,8b}$ = 12.0 Hz, 1H, H-8a), 4.39 (d, J = 9.5 Hz, 1H, H-6), 4.27 (dd, $J_{8a,8b}$ = 12.0 Hz, $J_{7,8b}$ = 6.7 Hz, 1H, H-8b), 3.75 (dd, J = 15.6, 6.7 Hz, 1H, H-1a′), 3.49 (dd, J = 15.2, 6.7 Hz, 1H, H-1b′), 2.39 (dd, $J_{3eq,3ax}$ = 11.8 Hz, $J_{3eq,4}$ = 4.0 Hz, 1H, H-3eq), 1.98 (t, $J_{3eq,3ax} \approx J_{3ax,4} \approx$ 11.8 Hz, 1H, H-3ax), 2.07, 2.03, 1.98, 1.93 (all s, 12H, 4 × $COCH_3$), 1.60−1.52 (m, 2H, H-2ab′), 1.39−1.23 (m, 12H, H-3ab′, H-4ab′, H-5ab′, H-6ab′, H-7ab′, H-8ab′), 0.90 (t, J = 6.8 Hz, 3H, H-9′); ^{13}C NMR (100 MHz, MeOD) δ 172.54, 172.45, 171.7, 171.6 (4 × $COCH_3$), 102.3 (C-2), 72.0 (C-6), 70.0 (C-7), 69.7 (C-4), 66.1 (C-5), 65.4 (C-1′), 64.7 (C-8), 33.9 (C-3), 33.0, 31.0, 30.7, 30.5, 30.4, 27.2, 23.7 (C-2′, C-3′, C-4′, C-5′, C-6′, C-7′, C-8′), 20.7 (4 × $COCH_3$), 14.4 (C-9′); HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{25}H_{40}NaO_{12}$ 555.2412, found 555.2423; m/z [2 M + Na]$^+$ calcd for $C_{50}H_{80}NaO_{24}$ 1087.4932, found 1087.4953.

*4′-Methoxyphenacyl [2-[5-Amino-N-[(benzyloxy)carbonyl]-1-pentyl] 4,5,7,8-tetra-O-acetyl-3-deoxy-α,β-D-manno-oct-2-ulopyranosid]onic Acid (**33**).* Kdo glycoside **15** (25 mg, 32 μmol, 1.0 equiv) was dissolved in 90% AcOH(aq) (1.0 mL), and the solution was heated to 35 °C. Freshly activated zinc powder (170 mg) was added in portions over 2 h. The mixture was filtered over Celite and rinsed with a 90% AcOH(aq) solution (5 mL) and a solution of EtOH/EtOAc (4 × 10 mL, 1:1 v/v). The solvents were concentrated under reduced pressure to afford a residue that was purified by silica gel flash chromatography (DCM/MeOH 1:0 to 8:2) to give carboxylic acid **33** (17 mg, 85%) as a white amorphous powder: $[\alpha]_D^{20}$ = +35 (c 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.30 (m, 5H, C*H*-Ar), 5.29 (br s, 1H, H-5), 5.19 (dt, $J_{6,7}$ = 9.6 Hz, $J_{7,8a} \approx J_{7,8b} \approx$ 3.1 Hz, 1H, H-7), 5.16−5.00 (m, 4H, CH_2Ph, H-4, N*H*Cbz), 4.40−4.32 (m, 1H, H-8a), 4.26 (d, $J_{6,7}$ = 9.6 Hz, 1H, H-6), 3.80−3.73 (m, 1H, H-1a′), 3.65 (t, $J_{7,8a} \approx J_{7,8b} \approx$ 6.6 Hz, 1H, H-8b), 3.59−3.49 (m, 1H, H-1b′), 3.24−3.07 (m, 2H, H-5ab′), 2.41 (dd, $J_{3ax,3eq}$ = 12.3 Hz, $J_{3eq,4}$ = 4.3 Hz, 1H, H-3eq), 2.06 (t, $J_{3ax,3eq} \approx J_{3ax,4} \approx$ 12.3 Hz, 1H, H-3ax), 2.10, 2.07, 2.01, 1.98 (all s, 12H, 4 × $COCH_3$), 1.67−1.35 (m, 6H, H-2ab′, H-3ab′, H-4ab′); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 170.7, 170.2, 170.0 (4 × $COCH_3$), 136.5 (C-Ar), 128.6−128.3 (CH-Ar), 99.7 (C-2), 70.8 (C-6), 66.2 (C-7), 67.6 (C-4), 67.1 (CH_2Ph), 64.3 (C-5), 63.7 (C-1′), 62.9 (C-8), 41.2 (C-5′), 32.3 (C-3), 29.9, 29.3, 23.0 (C-2′, C-3′, C-4′), 20.93−20.88 (4 × $COCH_3$); HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{29}H_{39}NNaO_{14}$ 648.2263, found 648.2280.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01431.

NMR spectra for new compounds and computation results of reaction intermediates (PDF)

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Notes

The authors declare no competing financial interest.

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