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Intramolecular Aglycon Delivery Enables the Synthesis of 6-Deoxy-β-D-*manno*-heptosides as Fragments of *Burkholderia pseudomallei* and *Burkholderia mallei* Capsular Polysaccharide

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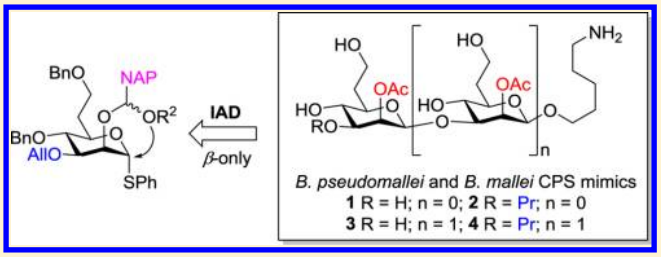
Supporting Information

ABSTRACT: *Burkholderia pseudomallei* and *Burkholderia mallei* are potential bioterrorism agents. They express the same capsular polysaccharide (CPS), a homopolymer featuring an unusual [→3)-2-*O*-acetyl-6-deoxy-β-D-*manno*-heptopyranosyl-(1→] as the repeating unit. This CPS is known to be one of the main targets of the adaptive immune response in humans and therefore represents a crucial subunit candidate for vaccine development. Herein, the stereoselective synthesis of mono- and disaccharidic fragments of the *B. pseudomallei* and *B. mallei* CPS repeating unit is reported. The synthesis of 6-deoxy-β-D-*manno*-heptosides was investigated using both inter- and intramolecular glycosylation strategies from thio-*manno*-heptose that was modified with 2-naphthylmethyl (NAP) at C2. We show here that NAP-mediated intramolecular aglycon delivery (IAD) represents a suitable approach for the stereocontrolled synthesis of 6-deoxy-β-D-*manno*-heptosides without the need for rigid 4,6-*O*-cyclic protection of the sugar skeleton. The IAD strategy is highly modular, as it can be applied to structurally diverse acceptors with complete control of stereoselectivity. Problematic hydrogenation of the acetylated disaccharides was overcome by using a microfluidic continuous flow reactor.



INTRODUCTION

Burkholderia pseudomallei and *Burkholderia mallei* are the causative agents of melioidosis[1,2] and glanders,[3] respectively. The clinical diagnosis of these diseases, which can affect both humans and animals, includes diverse manifestations that range from pneumonia and septicemia to skin abscesses.[4] Because of their high infectivity via the respiratory route and their intrinsic resistance to many common antibiotics, together with their low infectious doses and high mortality rates, *B. pseudomallei* and *B. mallei* are considered category B bioterrorism agents according to the U.S. Center for Disease Control and Prevention.[5] Recently, both pathogens have been added to a top-priority list among 13 "tier 1" selected agents and toxins by the U.S. Furthermore, it has been proven that *B. mallei* was used as a biological warfare agent during World Wars I and II, whereas the use of *B. pseudomallei* as a biological weapon was evaluated by the U.S. and the former Soviet Union.[6] The ease with which *B. pseudomallei* and *B. mallei* can be obtained, cultured, and disseminated (possibly on a large scale) makes the fight against these bacteria a serious public concern. Importantly, no human or veterinary clinical vaccines are currently available for immunization against melioidosis and glanders.[5]

For all of the aforementioned reasons, the development of an effective vaccine against *B. pseudomallei* and *B. mallei* has recently become an important research issue.[4,7] Over the last 2 decades, various experimental melioidosis and glanders vaccines have been tested in animal models, such as live-attenuated, killed whole-cell, and subunit vaccines, but only mitigated results have so far been obtained.[4,8−10] In the subunit vaccine category, there is strong evidence to suggest that the surface polysaccharides produced by *B. pseudomallei* and *B. mallei* are the main virulence factors that trigger the production of protective antibodies in humans.[11−14] As for Gram-negative bacteria, *B. pseudomallei* and *B. mallei* express high-molecular-weight capsular polysaccharides (CPS) at their surface that act as protective antigens. Interestingly, almost all virulent strains of *B. pseudomallei* and *B. mallei*, whether of human or animal origin, are known to express the same major CPS structure (type I O-PS), a homopolymer featuring an uncommon [→3)-2-*O*-acetyl-6-deoxy-β-D-*manno*-heptopyranose-(1→] as the repeating unit (Figure 1).[15−17] Consequently, it has been hypothesized that a CPS-based vaccine, if effective, could serve to immunize against both melioidosis and glanders infections.[17,18]

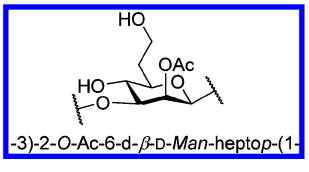


Figure 1. Structure of *B. pseudomallei* and *B. mallei* CPS homopolymer.

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Nevertheless, there are some severe issues associated with the isolation of polysaccharides from the large-scale culture of pathogenic *B. pseudomallei* and *B. mallei* bacteria, which require manipulation in biosafety level 3 laboratories.[7] The industrial production of such a CPS-based vaccine is also hampered by the tedious purification procedures required to produce pure CPS that is free of bacterial contaminants in sufficient quantities.[19] In recent years, organic synthesis has provided convenient processes by which to generate homogeneous carbohydrate antigens in a more reproducible manner.[20,21] The target sugar epitopes can be synthesized that display different lengths and feature suitable linkers at their reducing ends. They can be used to produce well-defined glycoconjugates and/or to study the minimal epitopes needed for recognition with protective antibodies.[22] For instance, the success of the Cuban anti-Hib CPS-based tetanus toxoid construct is a striking example of the advantages of organic synthesis for the development of glycoconjugate vaccines.[23]

From the organic chemistry perspective, the synthesis of the *B. pseudomallei* and *B. mallei* CPS repeating unit is challenging. The major difficulties are 3-fold: (1) the stereospecific formation of a 1,2-*cis*-manno glycosidic bond, (2) the C6 one-carbon homologation to generate a 6-deoxy-D-*manno*-heptose, and (3) the introduction of a labile acetyl group at C2. We report herein the chemical synthesis of the *B. pseudomallei* and *B. mallei* CPS repeating unit. Stereoselective synthesis of mono- and disaccharidic fragments (**1**–**4**) of (1→3)-linked 6-deoxy-2-*O*-acetyl-*β*-D-*manno*-heptopyranosides was studied using inter- and intramolecular glycosylation strategies. For the first time, we have successfully showed that the 2-naphthylmethyl (NAP)-mediated intramolecular aglycon delivery strategy is suitable for the complete stereocontrolled synthesis of 6-deoxy-*β*-D-*manno*-heptopyranosides without the need for rigid 4,6-*O*-cyclic protection.

RESULTS AND DISCUSSION

Synthetic Approach. In the core and surface polysaccharides of Gram-negative bacteria, L- and D-*glycero*-D-*manno*-heptoses of the *α*-anomeric configuration (1,2-*trans*) are ubiquitous.[24] Stereoselective syntheses of complex bacterial oligosaccharides incorporating these *α*-*manno*-heptoses have been achieved by taking advantage of the so-called neighboring group participation effect of having an acetyl at the C2 position.[25−31] Nevertheless, the synthesis of *β*-linked-*manno*-heptosides (1,2-*cis*)[32] still represents a major challenge. As far as we are aware, Crich and co-workers[33−35] are the only group to have reported the stereocontrolled synthesis of 1,2-*cis*-*manno*-heptosides in either the D- or L-*glycero* configurations. Their approach relies on a 4,6-*O*-alkylidene-type acetal donor that is required to achieve good *β*-stereoselectivity under donor preactivation conditions. The methodology was also extended to the preparation of 6-deoxy-*β*-D-*manno*-heptosides.[34,36] In order to do so, they devised a 4,6-*O*-[1-cyano-2-(2-iodophenyl)ethylidene] acetal-protected thioglycoside donor. After *β*-stereoselective glycosylation, the target glycoside was formed via a reductive radical fragmentation followed by an oxidative treatment with DDQ. Although this very elegant methodology represents pioneering work in the field, certain drawbacks are associated with its application to oligosaccharide synthesis. First, it necessitates the formation of a diastereoisomeric mixture of L- and D-*glycero*-*manno*-heptopyranoses prior to the synthesis of the 4,6-*O*-protected cyclic acetal. Second, the oxidative treatment with DDQ under aqueous conditions is not suitable for use with commonly used protecting groups such as PMB and NAP ethers. Third, the saponification step that is required to cleave the (2-cyanophenyl)acetyl ester resulting from the radical fragmentation is somewhat incompatible with the synthesis of partially acetylated carbohydrates, such as *B. pseudomallei* and *B. mallei* CPS fragments.

Intramolecular aglycon delivery (IAD)[37,38] is an alternative approach for the stereoselective synthesis of 1,2-*cis*-glycosides. IAD was originally pioneered by Hindsgaul[39] and Stork[40] to tackle the problem of *β*-D-mannoside synthesis. This method was further implemented by Ito and Ogawa,[41] who developed the PMB-[42−44] and NAP-mediated[45,46] IAD for the synthesis of challenging 1,2-*cis*-linkages. In this two-step protocol (Figure 2), a glycosyl donor equipped with a PMB or NAP group at the

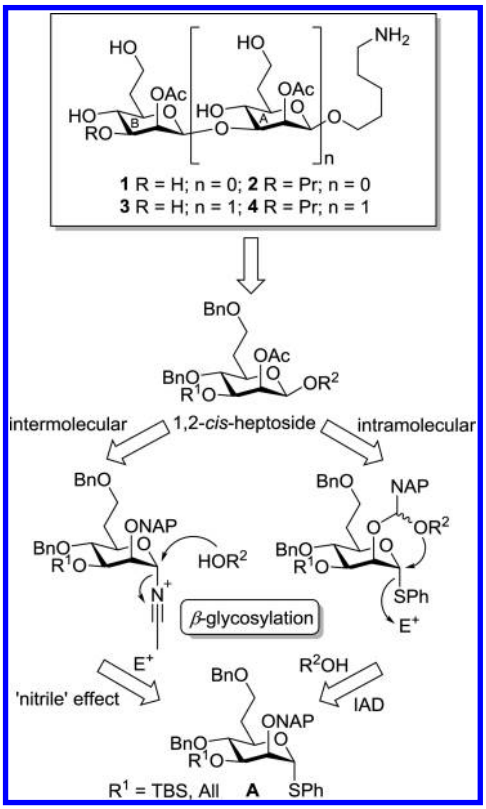

Figure 2. Retrosynthetic analysis of *B. pseudomallei* and *B. mallei* CPS fragments via inter- or intramolecular glycosylation.

C2 position and an alcohol acceptor are tethered using DDQ to form a mixed acetal via a single electron transfer mechanism. After activation of the anomeric position, the aglycon is stereoselectively delivered from the same side as the tether, yielding excellent if not exclusive *β*-anomeric selectivity in most substrates. In the case of our work, the IAD approach was particularly appealing because the regenerated free OH at the C2 position could be directly acetylated after the glycosylation step.

As depicted in Figure 2, monosaccharide **1** and disaccharide **3**, representing one or two repeating unit(s) of *B. pseudomallei* and *B. mallei* CPS, respectively, were chosen as targets. Because we were mindful of potential *trans* esterification[47,48] between the alcohols at C2 and C3 in the final compounds, we also planned to synthesize the corresponding C3 *O*-propylated compounds, **2** and **4**. In this manner, the acetyl migration would be avoided, and we reasoned that the propyl group could

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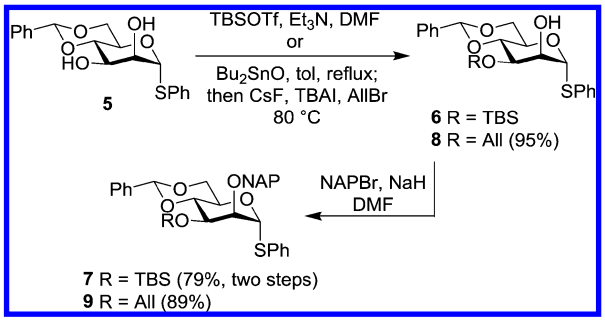
mimic the chain elongation/termination at the C3 position. The reducing-end anomeric positions of the target compounds were fixed in the β-configuration bearing an 5-amino-1-pentyl linker, which would further serve to anchor the CPS fragments to an immunogenic protein, such as CRM-197.[49] Intermolecular glycosylation with heptose donor **A** was also investigated considering that we could modulate the β-selectivity via the so-called "nitrile" effect.[50] NAP-mediated IAD[45] was favored over PMB owing to the superior yields typically obtained for the mixed acetals formation as well as the intramolecular glycosylation step.[38] Regarding heptose **A**, two different protecting groups at the C3 position, namely, TBS and allyl, were investigated. It was expected that both TBS and allyl groups could be selectively removed allowing further chain elongation at C3 to provide oligosaccharide fragments by iteration of the optimized 1,2-*cis*-glycosylation protocol. Moreover, a thiophenyl moiety was chosen at the anomeric position because it can be activated in the presence of soft electrophiles without affecting the protecting groups.[51]

Synthesis of 6-Deoxy-*manno*-heptose Donors. The synthesis of *manno*-heptose donors started with known 4,6-*O*-benzylidene thiomannoside **5**[52,53] (Scheme 1). The bulky TBS group was regioselectively introduced at C3 by reacting **5** with *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) in the presence of triethylamine (Et_3N). Subsequent reaction of crude product **6** with 2-(bromomethyl)naphthalene (NAPBr) in the presence of sodium hydride (NaH) gave **7**[54] in 79% yield over two steps. Allylation of **5** was accomplished with stannylene acetal chemistry[55] using dibutyltin(IV) oxide (Bu_2SnO) followed by treatment with allyl bromide (AllBr) at 80 °C to afford **8** in high yield (95%). The latter was protected at C2 with a NAP group under the aforementioned conditions to give **9** (89%). The regioselectivity of the reactions was confirmed by 2D NMR HMBC, which showed strong cross-peak correlations between CH_2NAP and C2.

Scheme 1. Regioselective Synthesis of Mannose Derivatives 7 and 9

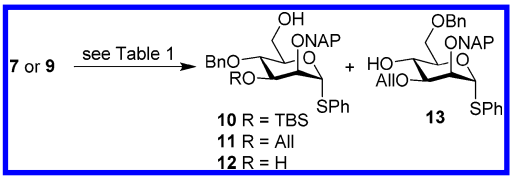


The regioselective reductive ring opening of the benzylidene acetals[56,57] in **7** and **9** to provide primary alcohol derivatives **10** and **11** was examined next (Table 1). Reaction of **7** with boron tetrahydrofuran complex (BH_3·THF) in the presence of catalytic amounts of scandium(III) triflate[58] [$Sc(OTf)_3$] led to desired alcohol **10** in 30% yield along with concomitant TBS deprotection (entry 1). Substitution of $Sc(OTf)_3$ with trimethylsilyl trifluoromethanesulfonate (TMSOTf)[59] led to **10** being produced in a much improved yield of 89% without affecting the TBS group (entry 2). DIBALH/tol-mediated reduction[60] of **7** furnished **10** in only 14% yield along with 3,6-diol **12** and unreacted starting material (entry 3). Ring opening of benzylidene acetal **9** was then attempted using BH_3·THF (entry 4); however, predominant hydroboration of the double bond led to decomposition. Reaction of **9** with DIBALH/tol under diluted conditions was sluggish, affording expected regioisomer **11** in 41% (entry 6). More gratifying results were obtained when **9** was treated with DIBALH/tol without diluting the substrate (entry 7). Under these conditions, **11** was formed in 73% yield along with its regioisomer, **13** (15%), in an inseparable mixture.

The C6 one-carbon homologation of derivatives **10** and **11** was then studied (Scheme 2). Two different synthetic approaches have been described in the literature for the chain elongation toward 6-deoxy-D-*manno*-heptoses.[26] The strategy developed by Borén and co-workers[61] involved the Wittig reaction of the C6 aldehyde group with methoxymethylene-triphenylphosphorane followed by acid hydrolysis. In another approach, Aspinall and co-workers[62,63] displaced a 6-*O*-triflate or mesylate group with cyanide ions followed by reduction with DIBALH and acid hydrolysis. The latter strategy was adopted for this project.

Therefore, alcohol **10** was treated with triflic anhydride (Tf_2O) in the presence of 2,6-lutidine. Unexpectedly, the

Table 1. Regioselective Reductive Ring Opening of Benzylidene Acetals 7 and 9



entry	compd	reagent(s)	solvent	T (°C)	time (h)	yield (%)[a] 10 or 11	yield (%)[a] 13
1	7	BH_3·THF/$Sc(OTf)_3$	DCM	23	21	30[b]	[c]
2	7	BH_3·THF/TMSOTf	DCM	23	3	89	[c]
3	7	DIBALH/tol	DCM	−78 to 23	24	14[b,d]	[c]
4	9	BH_3·THF[e]	DCM	23	0.5	[c]	[c]
5	9	DIBALH/DCM[e]	neat	−10 to 23	2	[c]	[c]
6	9	DIBALH/tol	tol	−10 to 23	24	41[f]	5[f]
7	9	DIBALH/tol	neat	−10 to 23	3	73[f]	15[f]

[a]Isolated yield. [b]3,6-Diol **12** was obtained as the major compound. [c]Not detected. [d]Starting material was recovered in 25% yield. [e]Decomposition of the starting material, leading to a complex mixture. [f]Obtained as an inseparable mixture. Ratio was estimated by ^{1}H NMR.

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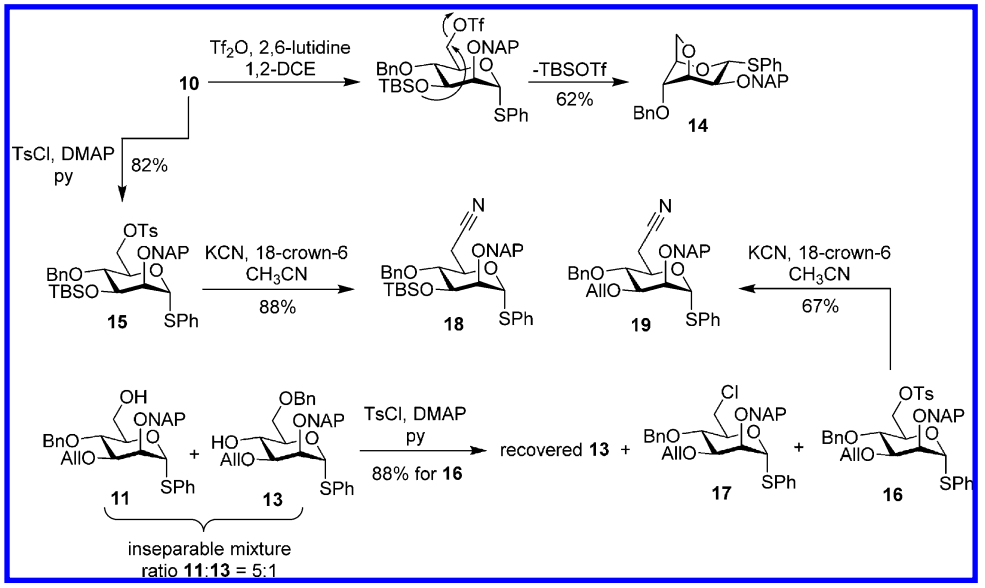
Scheme 2. C6 One-Carbon Homologation toward Nitrile Derivatives 18 and 19



corresponding triflate derivative was converted in situ into more stable 3,6-anhydro-mannose **14** in 62% yield, releasing TBSOTf in the process. The $^{3}J_{1,2}$ coupling constant of 8.0 Hz in the ^{1}H NMR spectra of **14** indicated a $^{1}C_{4}$ conformation. The formation of 3,6-anhydro-mannose is not unprecedented, as Kovac[64] and Lowary[65] isolated similar compounds under fluorinating conditions. By contrast, when allyl derivative **11** was treated with Tf_2O, only decomposition occurred and no anhydro-mannose was isolated. To circumvent this problem, tosylation[27] of **10** with tosyl chloride (TsCl) in the presence of catalytic DMAP in pyridine afforded compound **15** in 82% yield. The mixture of regioisomers **11** and **13** was tosylated under the same conditions. At this step, secondary alcohol **13** did not react with TsCl; therefore, compounds **13** and **16** (88%) were readily separable by flash chromatography. The formation of chlorinated compound **17** was observed as a side product when the reaction was run at high temperature. S_N2 reaction of tosylated **15** and **16** proceeded without complication by using potassium cyanide (KCN) together with 18-crown-6 in anhydrous CH_3CN (88% for **18**, 67% for **19**).[27]

A three-step reduction of nitriles into C7 primary alcohols was then investigated. As depicted in Scheme 3, nitrile derivatives **18** and **19** were reduced with DIBALH at cryogenic temp (−78 °C). Interestingly, the $(i\text{-Bu})_2$Al-imine complex was detected by LRMS. After acidic hydrolysis (THF/1 N HCl(aq) 9:1) of the imine, the resulting aldehydes were reduced to desired alcohols **20** and **21** with sodium borohydride ($NaBH_4$). When nitrile **18** was subjected to this procedure (Table 2), only moderate yields of alcohol **20** were obtained (33−60%, entry 1). These yields, however, were not reproducible, and cleavage of the TBS group occurred predominantly. Better results were obtained with allyl derivative **19**, which afforded **21** in 87% yield when using 1.2 equiv of DIBALH/tol (entry 2). It is noteworthy that acidic hydrolysis with THF/1 N HCl was crucial in order to convert all of the imine into aldehyde; otherwise, **21** was formed in lower yield (56%, entry 3). Moreover, use of DIBALH in DCM mainly led to degradation of **19** into primary amine **22**, as detected by LRMS (entry 4).

Subsequent benzylation of the C7 primary alcohol in **20** was not as straightforward as expected (Table 3). Under standard

Scheme 3. Three-Step Nitrile Conversion to C7 Primary Alcohols 20 and 21

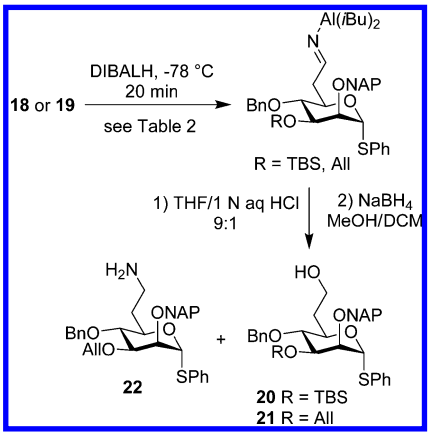


Table 2. Optimization of Nitrile Reduction Using DIBALH

entry	compd	reagent (1.2−1.5 equiv)	solvent	yield (%)[a]
1	**18**	DIBALH/tol	tol	33−60[b]
2	**19**	DIBALH/tol	tol	87
3	**19**	DIBALH/tol	tol	56[c]
4	**19**	DIBALH/DCM	DCM	[d]

[a]Isolated yield in alcohol **20** or **21** (over three steps from **18** or **19**). [b]Yields were not reproducible, and unidentified byproducts were formed. [c]Crude was dissolved in EtOAc and washed with 1 N HCl (3×) instead of reacting it for 1 h with THF/1 N HCl. [d]Degradation occurred. Amine **22** was detected by LRMS (m/z 556 $[M + H]^+$).

conditions (NaH, BnBr), derivative **23** was formed in 50% yield at best along with alcohol **24** (20%) because of the partial cleavage of the TBS group (entry 1). We then tried using neutral conditions of silver(I) oxide (Ag_2O), but **23** was isolated in 36% yield along with **24** (12%) and unreacted **20** (entry 2). In contrast, benzylation of allyl derivative **21** gave a nearly quantitative yield of 97% without formation of **24** when standard conditions (NaH, BnBr) were used.

To summarize this section, novel 6-deoxy-D-*manno*-heptose donors **23** and **25** were synthesized in nine linear steps from

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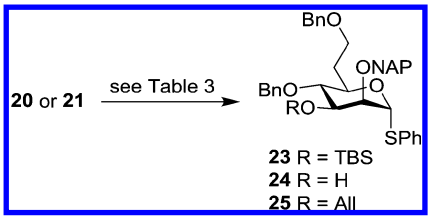
Table 3. Primary Alcohol Benzylation for the Synthesis of Mannoheptoses 23 and 25



entry	compd	reagents	yield (%)[a] 23 or 25	24
1	**20**	BnBr, NaH, DMF	50[b]	20
2	**20**	BnBr, Ag_2O, DCM	36	12
3	**21**	BnBr, NaH, DMF	97	[c]

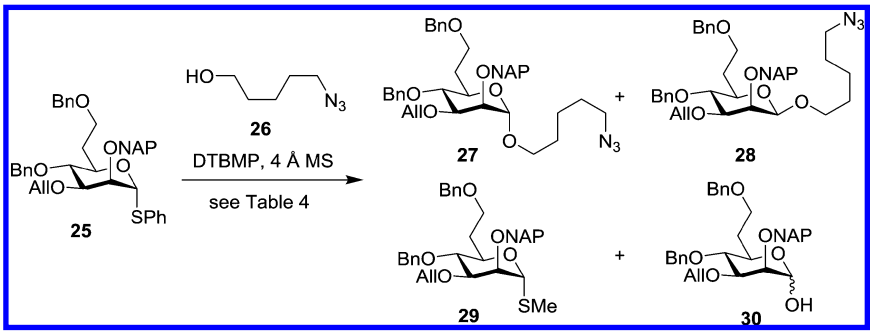
[a]Isolated yield. [b]Yields were not reproducible. [c]Not detected.

known diol **5**. Superior overall yields were obtained for allyl derivative **25** (35%) compared to that of TBS derivative **23** (15%), which could be attributed to the increased stability of the allyl group under both reductive and acidic conditions. Throughout this robust synthetic sequence, we were able to routinely prepare gram quantities of **25** (~5 g), which was stable for several months when stored at −20 °C. Thus, optimization of the inter- and intramolecular glycosylation conditions were preferentially performed with derivative **25** with the knowledge that under Pd-catalyzed hydrogenation the allyl group could be converted into target C3 *O*-propylheptose derivatives **2** and **4**.

Intermolecular Glycosylation. With heptose **25** in hand, we next planned to study its stereoselective behavior as a donor under standard intermolecular glycosylation conditions with azidopentyl acceptor **26**[66] (Table 4). Different thioglycoside promoter systems were screened, such as dimethyl(methylthio)sulfonium trifluoromethanesulfonate (DMTST),[67] *p*-nitrobenzenesulfenyl triflate (*p*-NO_2PhSOTf),[68] and dimethyl disulfide (Me_2S_2)/Tf_2O[69] together with 4 Å molecular sieves as well as the hindered base 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP); the latter acts as an acid-scavenger. Other well-known promoter systems, such as NIS/triflic acid (TfOH), NIS/silver trifluoromethanesulfonate (AgOTf), iodine dicollidine perchlorate (IDCP), and IBr, could not be employed because of the incompatibility of the allyl group in **25** with iodonium ions. We first tried a normal activation procedure in which **25** and **26** were premixed before adding the promoter (entries 1−5). Glycosylation with DMTST in DCE from −10 to 40 °C afforded predominantly *α*-anomer **27** (48%) along with *β*-anomer **28** (35%) (entry 1). The mixture was readily separable by silica gel chromatography. The stereochemistry of the anomeric linkages was assigned on the basis of undecoupled 2D NMR HSQC $^1J_{C1,H1}$ coupling constants (168 Hz for **27**; 154 Hz for **28**). In order to increase the diastereoselectivity toward the *β*-anomer, acetonitrile was added in the reaction to take advantage of the *β*-stereodirective nitrile effect.[50] Unfortunately, no significant improvements were observed using a 2:1 DCE/CH_3CN solvent mixture (entry 2), whereas a slight increase in *β*-selectivity occurred in neat CH_3CN (90%, ratio **27**/**28** ~ 1.0:1.1, entry 3). No glycosides were formed under the promotion of *p*-NO_2PhSOTf, as **25** was almost totally recovered (entry 4). Activation of **25** using Me_2S_2/Tf_2O only provided trace amounts of heptosides **27** and **28** (entry 5).

Preactivation conditions[70] were then assessed at −78 °C in which donor **25** was activated with different promoters prior to adding acceptor **26** to the mixture (entries 6−9). We reasoned that this protocol could favor the in situ formation of a transient *α*-anomeric triflate[71,72] and allow the synthesis of *β*-heptoside **28** in increased yields via an S_N2-like reaction.[73] Similar to the

Table 4. Intermolecular Glycosylation of Thiodonor 25 with Azide 26 with or without Donor Preactivation



entry	reagent(s)	solvent	*T* (°C)	time (h)	yield (%)[a] 27	28
1[b]	DMTST[c]	DCE	−10 to 40	2	48	35
2[b]	DMTST[c]	DCE/CH_3CN 2:1	−10 to 40	2	48	38
3[b]	DMTST[c]	CH_3CN	−10 to 23	5	**42**	**48**
4[b]	*p*-NO_2PhSOTf[d]	DCE	−10 to 40	24	[e]	[e]
5[b]	Me_2S_2/Tf_2O	DCE	−10 to 40	1	trace	trace
6[f]	*p*-NO_2PhSOTf[d]	DCM	−78 to 40	24	[e]	[e]
7[f]	Me_2S_2/Tf_2O	DCM	−78 to −30	3	[g,h]	[g,h]
8[f]	DMTST[c]	DCM	−78 to 23	16	49	32
9[f]	Ph_2SO/Tf_2O	DCM	−78	2	[g]	[g]

[a]Isolated yield. [b]Normal procedure without donor preactivation. [c]DMTST was formed in situ by reacting Me_2S_2 (3.0 equiv) and MeOTf (3.0 equiv). [d]*p*-NO_2PhSOTf was formed in situ by reacting *p*-NO_2PhSCl (1.2 equiv) and AgOTf (2.5 equiv). [e]No reaction. [f]Donor preactivation protocol. [g]Donor degradation into hemiacetal **30** occurred. [h]Thiomethyl glycoside **29** was isolated as a minor compound (18%).

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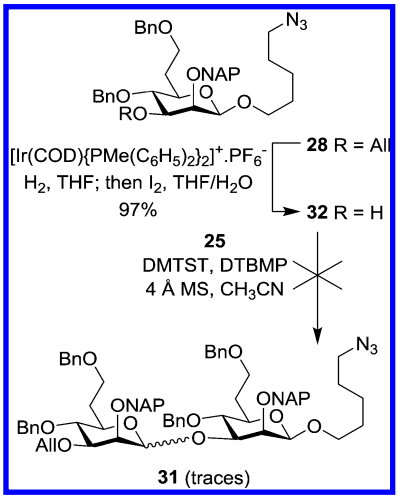
normal procedure, p-NO_2PhSOTf did not allow the activation of donor **25** (entry 6). Preactivation under the promotion of Me_2S_2/Tf_2O led to degradation of **25** along with a minor compound whose structure was assigned to α-thiomethyl glycoside **29** (18%, $^1J_{C1,H1}$ = 165 Hz, entry 7). This compound could come from S-glycosylation between activated donor **25** and methanethiol, which is formed in situ by the reaction of acceptor **26** with highly reactive intermediate CH_3STf. Preactivation with DMTST did not proceed successfully at −78 °C; yield and selectivity comparable with the normal procedure were obtained when the reaction was performed at rt (entry 8). The powerful diphenylsulfoxide $(Ph_2SO)/Tf_2O$[74] promoter system was also explored under preactivation conditions, but unfortunately, donor degradation occurred predominantly (entry 9).

Although the intermolecular glycosylation strategy provided somewhat low β-stereoselectivities, the good overall yield (90%) obtained with the normal procedure prompted us to apply the optimized conditions to the formation of disaccharide **31** (Scheme 4). Deallylation of **28** under Ir-catalyzed[75]

Scheme 4. Attempt To Synthesize Disaccharide 31 via an Optimized Intermolecular Glycosylation Reaction



conditions afforded **32** in excellent yield (97%). Unfortunately, glycosylation of acceptor **32** with thiodonor **25** under DMTST promotion in acetonitrile gave only trace amounts of disaccharide **31** even after forcing the conditions (6.0 equiv DMTST, reflux, 24 h). Acceptor **32** was almost fully recovered after the reaction together with hydrolyzed donor **30**. This coupling incompatibility between **25** and **32** could be due to the unfavorable steric interactions between the two NAP groups at C2. At this point, no further optimization of the intermolecular process was undertaken, and synthetic efforts were exclusively focused toward the IAD approach.

Intramolecular Glycosylation. Formation of mixed acetals between heptose derivatives and aminolinkers was the first step of the IAD protocol (Scheme 5). Thus, heptoses **23** or **25** were reacted with alcohols **26** or **40**[76] in the presence of DDQ (1.2 equiv) and 4 Å MS in DCM at rt. Good to excellent yields (62−81%) of mixed acetals **33**−**35** were isolated within short reaction times (2−3 h). Other solvents (tol, CH_3CN, THF, and DMF) were screened, but reactions were sluggish and gave decreased yields. A reaction was also performed that used CAN instead of DDQ as the oxidizing agent, but no acetal formation occurred. A series of acceptors were then selected, such as primary (**41**), secondary (**42** and **43**), and tertiary (**44**) alcohols, in order to evaluate the scope of the reaction. Good to excellent yields were achieved with diacetone galactose (**36**, 62%) and diacetone glucose (**37**, 83%), whereas the reaction with the more hindered stigmastanol (**43**) and 1-adamantanol (**44**) provided acetals **38** and **39** in moderate yields (40−44%). The rather low isolated yields obtained for acetals **38** and **39** were mainly due to instability toward purification on silica gel because conversions were almost complete according to TLC. Moreover, degradation of acetals **33**, **34**, **38**, and **39** occurred in deuterated solvents ($CDCl_3$ and/or py-d_5) during extensive ^{1}H and ^{13}C NMR analysis. Noteworthy, acetals were always formed in an inseparable R/S mixture with a predominance for the S diastereoisomer (R/S ratio of 1:4 for **36**), based on 2D NMR NOE correlations together with the empirical rules previously reported by Ito.[43]

Mixed acetals **33**−**35** were then subjected to the IAD reaction under different activating conditions (Table 5). Glycosylations were usually performed in diluted DCE at 40 °C in the presence of 5 Å molecular sieves in conjunction with hindered base DTBMP, which has been shown to be a crucial acid scavenger throughout the IAD process.[38] When methyl trifluoromethanesulfonate (MeOTf) was used as the promoter, degradation of tethers **33** and **34** predominantly occurred (entries 1 and 2). Cleavage of the TBS group in **33** was also detected by LRMS. Changing MeOTf to p-NO_2PhSOTf provided somewhat improved results, as target β-heptoside **46** was isolated as a single anomer, albeit in low yield (16%, entry 3). Other isolated products consisted mainly of the degradation product of tether **34** and unreacted starting material. Under the promotion of DMTST, the acetals were found to be more stable throughout the IAD process, and increased yields of β-*manno*-heptosides **46** (45%) and **47** (62%) were obtained with complete β-stereoselectivity; no α-heptosides were isolated or detected by NMR (entries 4 and 5). The efficiency of the intramolecular glycosylation was strongly solvent-dependent (entries 6−9). It was observed that switching DCE to CH_3CN or toluene had a detrimental effect on the yields, whereas in THF, acetal **35** was degraded. Moreover, no reaction occurred in DMF, and the starting material was fully recovered. It was also observed that the reaction rate and formation of byproducts were modulated by the nature of the molecular sieves, namely, 4 or 5 Å MS. Indeed, identical experiments using 4 Å MS accelerated the reaction kinetic, providing **47** in decreased yield (36%, entry 10). During the latter reaction, α-(1→2)-linked disaccharide **49** was also isolated as a minor byproduct. It can be postulated that **49** originated from the intermolecular glycosylation of β-*manno*-heptoside **47** with hydrolyzed acetal **48**, which was detected in the reaction mixture.

We then applied the optimized IAD conditions to more complex acetals (Scheme 6). Complete β-stereoselectivities ($^1J_{C1,H1}$ = 155−158 Hz) were achieved in all cases with yields ranging from 46 to 75% for heptosides **47**, **50**, **51**, and **53**. Adamantanyl acetal **38** was, however, unstable under these conditions and underwent hydrolysis to alcohol **48**; only trace amounts of β-heptoside **52** were detected. Therefore, instead of starting from purified acetals (route A), the IAD reaction was performed on the crude acetals mixture in order to minimize degradation (route B). Under these conditions, adamantanyl β-heptoside **52** was isolated in a satisfying 58% yield over two steps. This one-pot procedure proved to be efficient for the synthesis of heptosides **47**, **50**, and **52**, although similar overall

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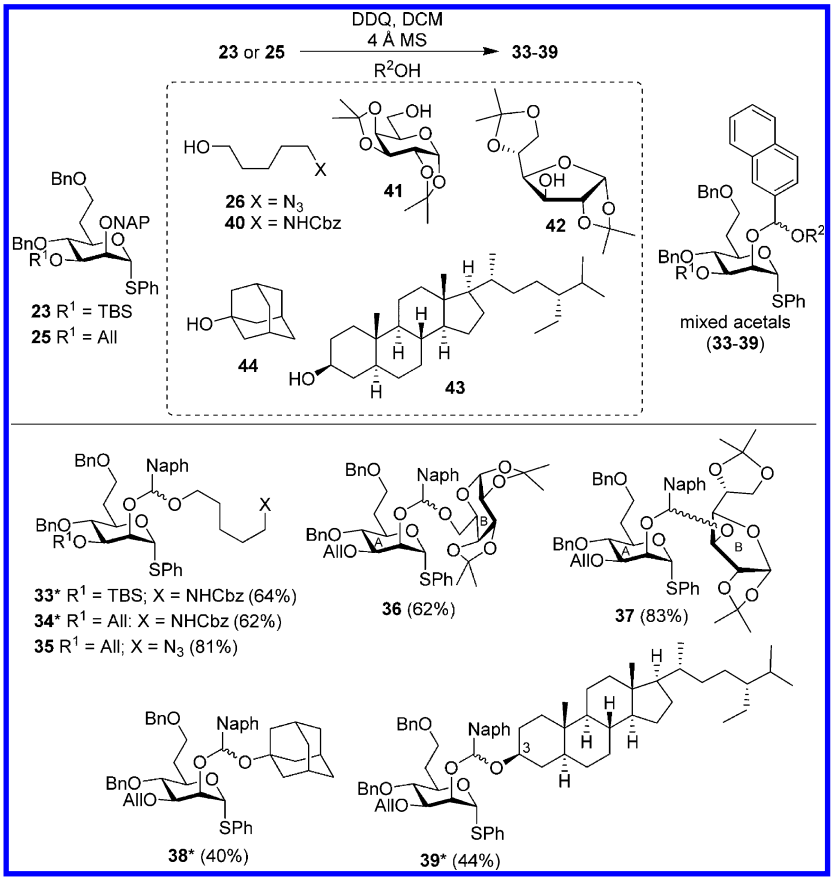
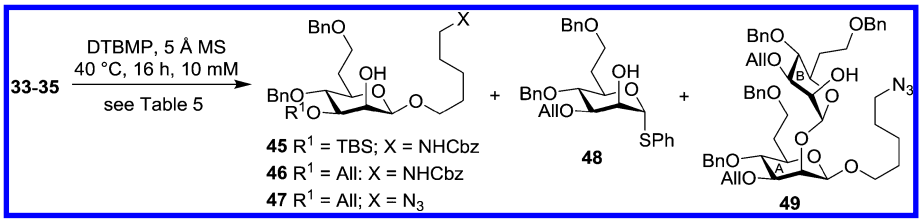
Scheme 5. Synthesis of Mixed Acetals 33−39[a]



[a]Acetals with an asterisk were unstable and degraded in $CDCl_3$ and/or py-d_5 during NMR analysis. Naph = naphthyl.

Table 5. Optimization of the IAD Reaction with Acetals 33−35



					yield (%)[a]	
entry	compd	reagent	solvent	product	β	α
1	33	MeOTf	DCE	45	25	[b]
2	34	MeOTf	DCE	46	[c]	
3	34	*p*-NO_2PhSOTf[d]	DCE	46	16	[b]
4	34	DMTST[e]	DCE	46	45	[b]
5	35	DMTST[e]	DCE	47	**62**	[b]
6	35	DMTST[e]	CH_3CN	47	35	[b]
7	35	DMTST[e]	toluene	47	12	[b]
8	35	DMTST[e]	THF	47	[c]	
9	35	DMTST[e]	DMF	47	[f]	
10	35	DMTST[e,g]	DCE	47	36[h]	[b]

[a]Isolated yields. [b]Not detected. [c]Acetal decomposition occurred leading to alcohol 48 as the major compound. [d]*p*-NO_2PhSOTf was formed in situ by reacting *p*-NO_2PhSCl (1.2 equiv) and AgOTf (2.5 equiv). [e]DMTST was formed in situ by reacting Me_2S_2 (3.0 equiv) and MeOTf (3.0 equiv). [f]No reaction. [g]Reaction was performed with 4 Å MS for 2 h. [h]Disaccharide **49** was isolated as a byproduct.

yields were achieved for heptosides **51** and **53**. Notably, the exclusive β-stereoselectivity achieved for the NAP-mediated IAD reaction of 6-deoxy-*manno*-heptosides is rather unusual because similar work with mannosides highlighted the importance of 4,6-*O*-cyclic protection to reach high β-stereoselectivity.[42,54] Recently, Ito and co-workers[46] have also reported the synthesis of β-mannosides with complete control

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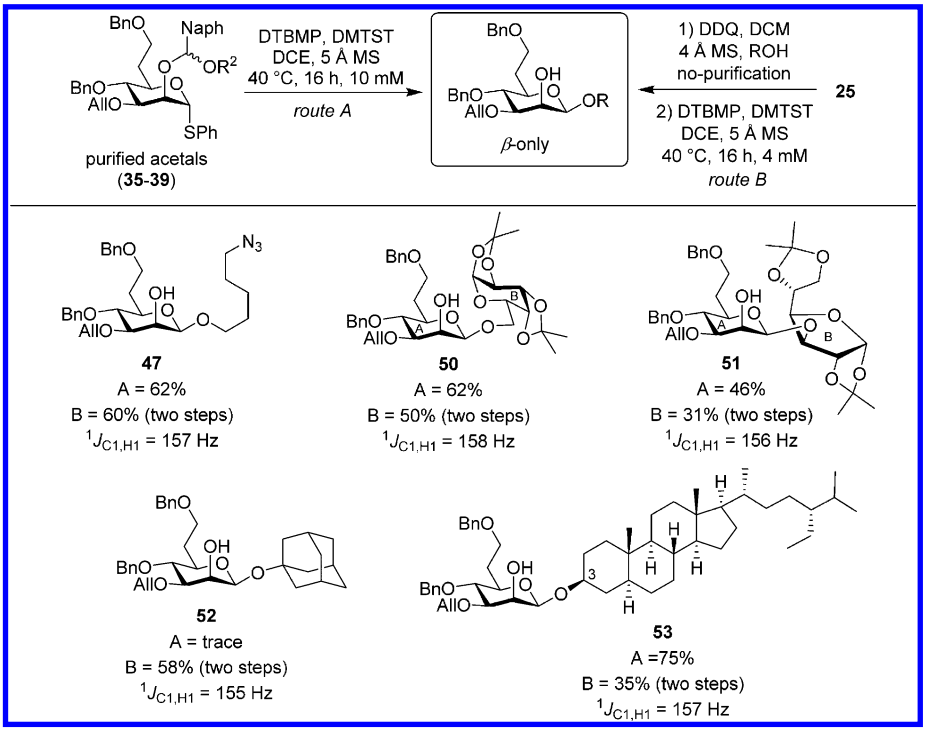
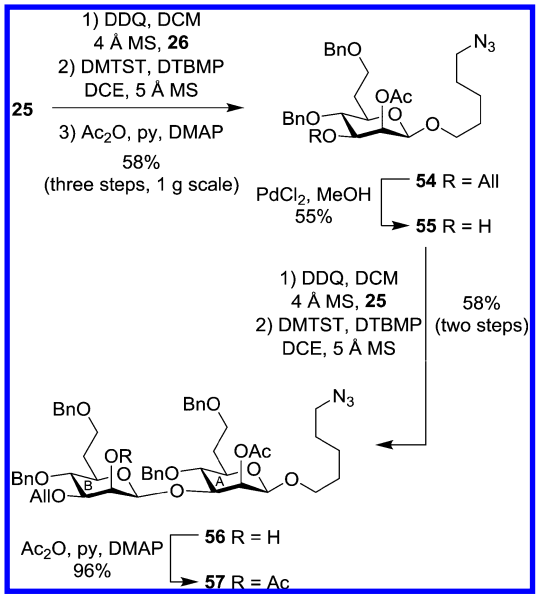
Scheme 6. Scope of the IAD Approach



of stereoselectivity through NAP-mediated IAD using 3,4,6-tri-*O*-benzylated donors.

Having shown that the IAD approach was suitable for the synthesis of diverse β-heptosides, we undertook the synthesis of disaccharidic *B. pseudomallei* and *B. mallei* CPS mimics **3** and **4** (Scheme 7). First, the IAD reaction was scaled up to 1 g, affording heptoside **54** in 58% yield over three steps upon acetylation of crude alcohol **47**. Ir-catalyzed deallylation of **54** provided only low and nonreproducible yields of alcohol **55** (<50%), which was presumably due to the catalyst deactivation with trace pyridine found in **54**. Deallylation of **54** using stoichiometric palladium(II) chloride ($PdCl_2$) in MeOH gave alcohol **55** in 55% yield. At this stage, acetyl migration from the C2 to the C3 position could not be avoided (ratio C2/C3 ∼ 4:1). Therefore, in order to minimize *trans* esterification, alcohol **55** was not purified but was directly coupled with an equimolar amount of thiodonor **25** using the optimized one-pot IAD protocol. In this way, disaccharide **56** was obtained in 58% yield with complete β-selectivity ($^1J_{C1',H1'}$ = 159 Hz). The free alcohol in **56** was then acetylated to give **57** (96%). The byproducts of the IAD reaction mainly consisted in the formation of C2 alcohol **48** and unreacted acceptor **55** coming from the decomposition of the naphthaldehyde acetal. No (1→2)-linked disaccharide was isolated from the reaction mixture.

Scheme 7. Synthesis of Disaccharide 57 by Optimized IAD Reaction



Final Deprotection of Mono- and Diheptosides. Pd-catalyzed hydrogenation of monosaccharides **55** and **54** cleanly yielded target heptosides **1** and **2**, respectively, in the form of their hydrochloride salts (Scheme 8). Importantly, Pd black together with 1.0 equiv of HCl were needed for complete deprotection. Indeed, hydrogenation was incomplete even after a long reaction time (>48 h) with catalysts such as Pd/C or $Pd(OH)_2/C$, whereas the use of a higher amount of HCl (>1.0 equiv) led to partial deacetylation. 1D and 2D NMR analysis of heptoside **1** showed that the acetyl group partially migrated from C2 (**1a**) to C3 (**1b**) (ratio of **1a**/**1b** ∼ 1.7:1.0 in D_2O). Such acetyl migration was recently observed by Wong and co-workers in the synthesis of partially C2 acetylated β-(1→4)-linked oligomannose derivatives.[48]

Deallylation of disaccharide **57** under standard conditions ($PdCl_2$, MeOH/DCE) gave **58** (69%). Contrary to monosaccharide **55**, no acetyl migration occurred in **58**, even after silica gel chromatography, as revealed by ^1H NMR. Unexpectedly, hydrogenolysis of disaccharides **57** and **58** into target heptosides **3** and **4** was found to be highly problematic. Incomplete deprotection of the four benzyl groups occurred using common catalysts such as Pd/C, $Pd(OH)_2/C$ and Pd black in various solvents including MeOH, THF, and AcOH as well as in mixtures of the latter. Furthermore, performing the

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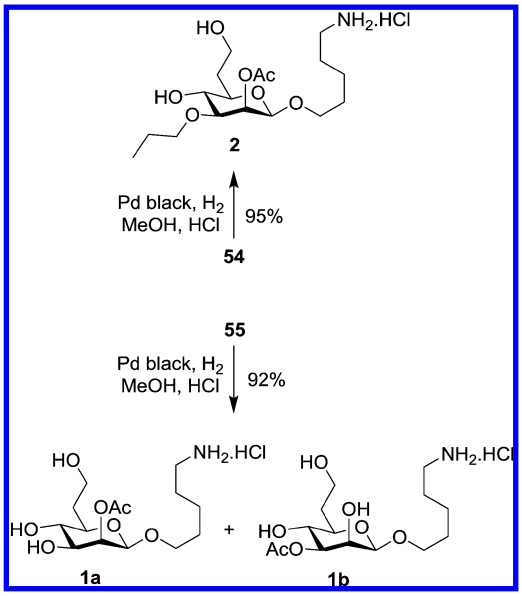
Scheme 8. Global Deprotection of Monosaccharides 54 and 55

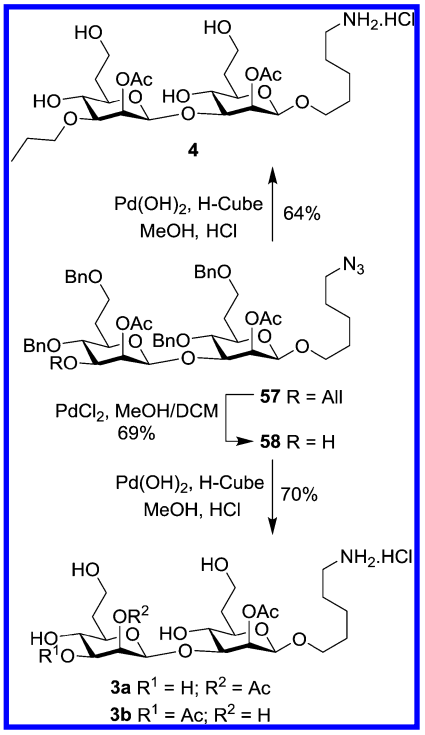


hydrogenation under pressure (6 bar) did allow complete debenzylation using Pd black in MeOH/THF/AcOH (2.0:1.0:0.3). However, methylation occurred on the free amine as well as other nonidentified side reactions, providing only trace amounts of target compounds. We hypothesized that the amine generated during the hydrogenation process was poisoning the catalyst and consequently dramatically decreasing the rate of debenzylation. Similar problems were encountered by Lowary and co-workers during the hydrogenation of an L-*gluco*-heptopyranose featuring a 8-azido-1-octyl chain and four benzyl groups.[77] They managed to overcome this difficulty by performing a cumbersome four-step protocol involving (1) selective azide reduction, (2) amine protection into a NHTFA, (3) debenzylation, and (4) amine deprotection. This procedure was obviously not suitable for the synthesis of our targets because the NHTFA could not be selectively deprotected in the presence of acetyl groups. Therefore, we instead turned our attention to a microfluidic continuous flow hydrogenation reactor system. Gratifyingly, performing the hydrogenation reaction with the H-Cube system in the full-H_2 mode using Pearlman's catalyst cleanly produced disaccharidic heptosides **3** and **4** in the form of their HCl salts (Scheme 9). After only one run, complete debenzylation occurred without any side reactions on the free amine. As revealed by the ^{1}H NMR spectrum of heptoside **3**, intramolecular migration of the acetyl group between the C2′ (**3a**) and C3′ (**3b**) positions was unavoidable, and an almost 1:1 mixture of the **3a**/**3b** regioisomers was formed upon dissolution in D_2O (Figure 3). As expected, no acetyl transfer occurred for C3 *O*-propyl analogue **4**.

■ CONCLUSIONS

In this study, we successfully applied the NAP-mediated IAD reaction for the stereoselective synthesis of diverse 6-deoxy-*β*-D-*manno*-heptosides including four mono- and disaccharides representing, respectively, one and two repeating units of *B. pseudomallei* and *B. mallei* CPS homopolymer. Complete stereoselectivity was achieved for the glycosylation reaction using a newly developed thioheptose donor equipped with a

Scheme 9. Final Deprotection of Disaccharides 57 and 58



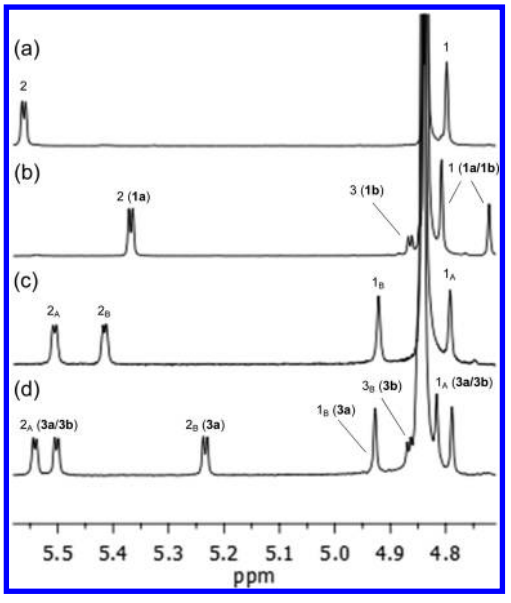


Figure 3. Selected area of the ^{1}H NMR spectra (500 MHz) of heptosides after dissolution in D_2O: (a) monosaccharide **2**; (b) monosaccharides **1a**/**1b**; (c) disaccharide **4**; and (d) disaccharides **3a**/**3b**.

NAP group at the C2 position. Notably, a rigid 4,6-*O*-benzylidene protection was not required to reach full *β*-selectivity. Global deprotection of disaccharides was problematic under standard hydrogenation conditions but was found to be effective under microfluidic conditions. The *B. pseudomallei* and *B. mallei* CPS fragments (**1**−**4**) were equipped with a 5-amino-1-pentyl linker at the anomeric position, enabling their subsequent conjugation with a carrier protein. This will allow the preparation of glycoconjugate vaccines that could elicit protective immune responses in vivo in mouse models of

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melioidosis and/or glanders. The synthesized heptosides could also be used to assess the minimal epitopes required for recognition with anti-CPS antibodies, work that 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 flame-dried glassware under an 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 or 5 Å molecular sieves were activated before use by heating 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 of $(NH_4)_6Mo_7O_{24}{\cdot}4H_2O$, 1.0 g of $Ce(NH_4)_4(SO_4)_4{\cdot}2H_2O$, 90 mL of H_2O, and 10 mL of H_2SO_4] with heating. Normal-phase flash column chromatography was performed on silica gel 60 Å (15−40 μm). Reversed-phase flash column chromatography was performed on C_{18} silica gel (25−40 μm). NMR spectra were recorded at 297 K in the indicated solvent ($CDCl_3$, MeOD, py-d_5, or D_2O) with a 400 or 500 MHz instrument, employing standard software provided by the manufacturer. ^{1}H and ^{13}C NMR spectra were referenced to tetramethylsilane (TMS, $\delta_H = \delta_C = 0.00$ ppm) as the internal reference for spectra in $CDCl_3$, MeOD, and py-d_5 or to external sodium 3-trimethylsilyl-(2,2,3,3-$^2H_4$)propanoate (TSP, $\delta_H = 0.00$ ppm) or 1,4-dioxane ($\delta_C = 67.19$ ppm) for spectra in D_2O. Assignments were based on ^{1}H, ^{13}C, DEPT-135, COSY, HSQC, undecoupled HSQC, HMBC, and NOESY experiments. Of the two magnetically nonequivalent geminal protons at C-6, the one resonating at lower field is denoted 6a and the one at higher field is denoted 6b. Interchangeable assignments are marked with an asterisk. High-resolution mass spectra (HRMS) were recorded on a ESI-Q-TOF mass spectrometer.

Phenyl 4,6-*O*-Benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-*O*-(2-naphthylmethyl)-1-thio-α-D-mannopyranoside (7). Diol **5**[52,53] (0.83 g, 2.3 mmol, 1.0 equiv) was dissolved in anhydrous DMF (5 mL), and the solution was cooled to −10 °C. Et_3N (0.35 mL, 2.5 mmol, 1.1 equiv) and TBSOTf (0.58 mL, 2.5 mmol, 1.1 equiv) were added, and the mixture was stirred for 2 h under N_2 while gradually being warmed to rt. The reaction was quenched by adding a saturated $NaHCO_3$(aq) solution (25 mL). DCM was added, and the organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to give phenyl 4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-1-thio-α-D-mannopyranoside (**6**) as a yellow solid: R_f 0.7 (PE/EtOAc 5:5); $[\alpha]_D^{20}$ = +148.3 (*c* 0.5, $CHCl_3$). To an ice-cold water solution of crude alcohol **6** (1.1 g, 2.3 mmol, 1.0 equiv) in anhydrous DMF (10 mL) was slowly added NaH (60% oil dispersion, 101 mg, 2.5 mmol, 1.1 equiv) under N_2, and the mixture was stirred for 20 min. NAPBr (611 mg, 2.8 mmol, 1.2 equiv) was then added, and the mixture was gradually warmed to rt. After being stirred for 3 h, the reaction was quenched with MeOH (3 mL) and diluted with EtOAc (40 mL). The organic layer was successively washed with water (3 × 50 mL) and brine (50 mL) and dried over $MgSO_4$, and the solutions were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/Et_2O 95:5 to 80:20) to give **7** (1.1 g, 79%, two steps) as a yellow oil: R_f 0.5 (PE/Et_2O 9:1); $[\alpha]_D^{20}$ = +62.7 (*c* 0.4, $CHCl_3$); HRMS (ESI-TOF) *m*/*z* [M + H]$^+$ calcd for $C_{36}H_{43}O_5SSi$, 615.2595; found, 615.2598. ^{1}H and ^{13}C NMR spectra data of **7**[54] were in agreement with those published in the literature.

Phenyl 3-*O*-Allyl-4,6-*O*-benzylidene-1-thio-α-D-mannopyranoside (8). To a solution of diol **5**[52,53] (1.0 g, 2.8 mmol, 1.0 equiv) in toluene (11 mL) was added Bu_2SnO (0.76 g, 3.1 mmol, 1.0 equiv), and the mixture was refluxed for 4 h using a Dean−Stark apparatus. The temperature was cooled to 80 °C, and then dried CsF (0.43 g, 2.8 mmol, 1.02 equiv), dried TBAI (1.23 g, 3.33 mmol, 1.2 equiv), and AllBr (0.3 mL, 3.3 mmol, 1.2 equiv) were successively added. After stirring for 24 h at 80 °C, the mixture was concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 95:5 to 80:20) to afford **8** (1.06 g, 95%) as a yellow oil: R_f 0.5 (PE/EtOAc 7:3); $[\alpha]_D^{20}$ = +227 (*c* 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53−7.26 (m, 10H, C*H*-Ar), 5.98−5.88 (m, 1H, H-2All), 5.62 (d, *J* = 1.0 Hz, 1H, H-1), 5.60 (s, 1H, C*H*-acetal), 5.33 (ddd, *J* = 17.3, 4.8, 1.6 Hz, 1H, H-3aAll), 5.23 (ddd, *J* = 10.3, 4.0, 1.4 Hz, 1H, H-3bAll), 4.35 (dd, *J* = 6.1, 1.3 Hz, 1H, H-1aAll), 4.33−4.31 (m, 2H, H-5, H-2), 4.24 (td, *J* = 6.1, 1.3 Hz, 1H, H-1bAll), 4.22−4.18 (m, 1H, H-6a), 4.12 (t, *J* = 9.5 Hz, 1H, H-4), 3.88 (dd, *J* = 9.1, 3.4 Hz, 1H, H-3), 3.84 (t, *J* = 10.4 Hz, 1H, H-6b), 2.84 (d, *J* = 1.3 Hz, 1H, O*H*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.6−133.5 (2 × C-Ar), 134.3 (C-2All), 131.7−126.1 (*C*H-Ar), 117.8 (C-3All), 101.8 (C-acetal), 87.9 (C-1), 79.1 (C-4), 75.4 (C-3), 72.2 (C-1All), 71.6 (C-5), 68.7 (C-6), 64.7 (C-2); HRMS (ESI-TOF) *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{25}O_5S$, 401.1417; found, 401.1417.

Phenyl 3-*O*-Allyl-4,6-*O*-benzylidene-2-*O*-(2-naphthylmethyl)-1-thio-α-D-mannopyranoside (9). To an ice-cold solution of alcohol **8** (8.6 g, 22 mmol, 1.0 equiv) in anhydrous DMF (47 mL) was slowly added NaH (60% oil dispersion, 0.95 g, 24 mmol, 1.1 equiv) under N_2, and the mixture was stirred for 20 min. NAPBr (5.7 g, 26 mmol, 1.2 equiv) was then added, and the mixture was gradually warmed to rt. After being stirred for 1 h, the reaction was quenched with MeOH (20 mL) and diluted with EtOAc. The organic layer was successively washed with water and brine and dried over $MgSO_4$, and the solutions were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 9:1 to 8:2) to furnish **9** (10.3 g, 89%) as a yellow oil: R_f 0.7 (PE/EtOAc 8:2); $[\alpha]_D^{20}$ = +63.1 (*c* 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88−7.18 (m, 17H, C*H*-Ar), 5.97−5.87 (m, 1H, H-2All), 5.64 (s, 1H, C*H*-acetal), 5.51 (d, *J* = 1.4 Hz, 1H, H-1), 5.31 (ddd, *J* = 17.3, 5.0, 1.6 Hz, 1H, H-3aAll), 5.20 (ddd, *J* = 10.4, 4.3, 1.5 Hz, 1H, H-3bAll), 4.94 (d, *J* = 12.4 Hz, 1H, C*H*HNAP), 4.89 (d, *J* = 12.4 Hz, 1H, C*H*HNAP), 4.38−4.26 (m, 3H, H-1aAll, H-4, H-5), 4.19 (dd, *J* = 10.2, 4.4 Hz, 1H, H-6a), 4.16−4.11 (m, 2H, H-1bAll, H-2), 3.95−3.86 (m, 2H, H-3, H-6b); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.4−132.1 (5 × C-Ar), 134.8 (C-2All), 131.9−126.1 (*C*H-Ar), 117.2 (C-3All), 101.7 (C-acetal), 87.6 (C-1), 79.2 (C-4), 78.2 (C-2), 76.1 (C-3), 73.4 (CH_2NAP), 72.2 (C-1All), 68.7 (C-6), 65.6 (C-5); MS (ESI-TOF) *m*/*z* 563.8 [M + Na]$^+$; HRMS (ESI-TOF) *m*/*z* [M + H]$^+$ calcd for $C_{33}H_{33}O_5S$, 541.2043; found, 541.2039.

Phenyl 4-*O*-Benzyl-3-*O*-*tert*-butyldimethylsilyl-2-*O*-(2-naphthylmethyl)-1-thio-α-D-mannopyranoside (10). To a solution of **7** (1.7 g, 2.8 mmol, 1.0 equiv) in anhydrous DCM (28 mL) were added BH_3·THF (1.0 M in THF, 10.5 mL, 10.5 mmol, 3.8 equiv) and TMSOTf (75 μL, 420 μmol, 0.15 equiv) under N_2. The mixture was stirred at rt for 3 h. The reaction was quenched with Et_3N (0.4 mL) and MeOH (10 mL). The solutions were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (pentane/EtOAc 9:1) to give **10** (1.5 g, 89%) as a yellow oil: R_f 0.4 (PE/EtOAc 8:2); $[\alpha]_D^{20}$ = +83.6 (*c* 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70−7.03 (m, 17H, C*H*-Ar), 5.30 (s, 1H, H-1), 4.81 (d, *J* = 12.0 Hz, 1H C*H*HNAP), 4.76 (d, *J* = 11.4 Hz, 1H, C*H*HPh), 4.66 (d, *J* = 12.0 Hz, 1H, C*H*HNAP), 4.48 (d, *J* = 11.4 Hz, 1H, C*H*HPh), 3.97−3.91 (m, 2H, H-5, H-3), 3.82−3.76 (m, 2H, H-2, H-4), 3.66−3.54 (m, 2H, H-6a, H-6b), 0.83 (s, 9H, C(CH_3)$_3$), 0.00 (s, 6H, 2 × CH_3Si); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5−133.2 (5 × C-Ar), 132.0−125.9 (*C*H-Ar), 86.9 (C-1), 81.0 (C-2), 75.9 (C-4), 75.3 (CH_2Ph), 73.8 (C-3), 73.8 (C-5), 73.6 (CH_2NAP), 62.3 (C-6), 26.1 (C(CH_3)$_3$), 18.2 (C(CH_3)$_3$), −4.2 (CH_3Si), −4.4 (CH_3Si); MS (ESI-TOF) *m*/*z* 634.7 [M + NH_4]$^+$, *m*/*z* 639.6 [M + Na]$^+$; HRMS (ESI-TOF) *m*/*z* [M + NH_4]$^+$ calcd for $C_{36}H_{48}NO_5SSi$, 634.3017; found, 634.3017.

Phenyl 3-*O*-Allyl-4-*O*-benzyl-2-*O*-(2-naphthylmethyl)-1-thio-α-D-mannopyranoside (11). To **9** (10.3 g, 19.1 mmol, 1.0 equiv) was added dropwise neat DIBALH (1.0 M in toluene, 140 mL, 140 mmol, 7.3 equiv) at −10 °C under N_2. The solution was then slowly warmed to rt. After being stirred for 3 h, the reaction mixture was poured into a cooled saturated aqueous K−Na-tartrate tetrahydrate

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solution and stirred vigorously for 2 h. The aqueous layer was extracted with EtOAc (450 mL), and the organic layer was washed with a saturated NH_4Cl(aq) solution (250 mL) and brine (250 mL). The solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 9:1 to 8:2) to give an inseparable mixture of regioisomers **11** and **13** (9.1 g, 88%, ratio **11**/**13** 4.9:1.0) as a white amorphous solid: R_f 0.5 (PE/EtOAc 8:2); $[\alpha]_D^{20}$ = +40.9 (*c* 0.1, $CHCl_3$); ^{1}H NMR of **11** (400 MHz, $CDCl_3$) δ 7.87−7.18 (m, 17H, C*H*-Ar), 6.01−5.87 (m, 1H, H-2All), 5.52 (s, 1H, H-1), 5.34 (dd, *J* = 17.3, 1.3 Hz, 1H, H-3aAll), 5.22 (d, *J* = 10.4 Hz, 1H, H-3bAll), 4.96 (d, *J* = 10.6 Hz, 1H, C*H*HPh), 4.89 (s, 2H, CH_2NAP), 4.67 (d, *J* = 10.6 Hz, 1H, C*H*HPh), 4.13−4.09 (m, 3H, H-1aAll, H-1bAll, H-5), 4.07 (s, 1H, H-2), 4.03 (t, *J* = 9.6 Hz, 1H, H-4), 3.85−3.78 (m, 3H, H-6a, H-6b, H-3); ^{13}C NMR of **11** (100 MHz, $CDCl_3$) δ 138.5−133.2 (5 × C-Ar), 134.7 (C-2All), 131.9−126.1 (*C*H-Ar), 117.4 (C-3All), 86.4 (C-1), 79.9 (C-3), 76.5 (C-2), 75.4 (*C*H_2Ph), 74.8 (C-4), 73.3 (C-5), 72.6 (*C*H_2NAP), 71.3 (C-1All), 62.4 (C-6); MS (ESI-TOF) *m*/*z* = 565.6 $[M + Na]^+$; HRMS (ESI-TOF) *m*/*z* $[M + NH_4]^+$ calcd for $C_{33}H_{38}NO_5S$, 560.2465; found, 560.2463.

Phenyl 3,6-Anhydro-4-*O*-benzyl-2-*O*-(2-naphthylmethyl)-1-thio-α-D-mannopyranoside (14). Tf_2O (88 μL, 0.52 mmol, 2.0 equiv) and 2,6-lutidine (66 μL, 0.58 mmol, 2.2 equiv) were dissolved in anhydrous DCE (2.7 mL), and the mixture was stirred at −10 °C under N_2. A solution of alcohol **10** (0.16 g, 0.26 mmol, 1.0 equiv) in anhydrous DCE (2.5 mL) was then added. The reaction mixture was stirred for 1 h at −10 °C and quenched with a saturated $NaHCO_3$(aq) solution (10 mL). The aqueous phase was extracted with DCM (3 × 15 mL). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was dissolved in anhydrous DCM (5 mL), and the mixture was refluxed for 2 h under N_2. The solutions were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (pentane/EtOAc 95:5 to 80:20) to provide **14** (77 mg, 62%) as a white sticky oil: R_f 0.30 (PE/EtOAc 9:1); $[\alpha]_D^{20}$ = +15.5 (*c* 0.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83−7.05 (m, 17H, C*H*-Ar), 5.13 (d, *J* = 8.8 Hz, 1H, H-1), 4.84 (d, *J* = 11.9 Hz, 1H, C*H*HNAP), 4.67 (d, *J* = 11.9 Hz, 1H, C*H*HNAP), 4.48 (d, *J* = 11.7 Hz, 1H, C*H*HPh), 4.45 (t, *J* = 2.7 Hz, 1H, H-5), 4.25 (d, *J* = 11.7 Hz, 1H, C*H*HPh), 4.18 (dd, *J* = 6.0, 1.2 Hz, 1H, H-3), 4.15 (d, *J* = 10.8 Hz, 1H, H-6a), 3.95 (dd, *J* = 10.8, 2.8 Hz, 1H, H-6b), 3.89 (dd, *J* = 6.0, 2.7 Hz, 1H, H-4), 3.78 (dd, *J* = 8.8, 1.2 Hz, 1H, H-2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.3−133.2 (5 × C-Ar), 132.2−126.1 (*C*H-Ar), 83.7 (C-1), 77.1 (C-4), 75.7 (C-3), 74.5 (C-5), 73.9 (C-2), 73.1 (*C*H_2NAP), 71.9 (*C*H_2Ph), 69.3 (C-6); HRMS (ESI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{30}H_{29}O_4S$, 485.1781; found, 485.1776.

Phenyl 4-*O*-Benzyl-3-*O*-*tert*-butyldimethylsilyl-2-*O*-(2-naphthylmethyl)-1-thio-6-*O*-tosyl-α-D-mannopyranoside (15). To a cooled solution (0 °C) of alcohol **10** (1.2 g, 1.9 mmol, 1.0 equiv) in anhydrous py (9.6 mL) were added TsCl (1.1 g, 5.7 mmol, 3.0 equiv) and DMAP (25 mg, 0.20 mmol, 0.1 equiv) under N_2. The mixture was stirred for 20 h, gradually warmed to rt, and diluted with EtOAc (60 mL). The organic phase was washed with a 10% HCl(aq) solution (2 × 25 mL), a saturated $NaHCO_3$(aq) solution (25 mL), and brine (25 mL). Solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 95:5 to 85:15) to provide **15** (1.2 g, 82%): R_f 0.5 (PE/EtOAc 7:3); $[\alpha]_D^{20}$ = +68.7 (*c* 0.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76−7.02 (m, 21H, C*H*-Ar), 5.38 (s, 1H, H-1), 4.79 (d, *J* = 10.8 Hz, 1H, C*H*HNAP), 4.77 (d, *J* = 12.0 Hz, 1H, C*H*HPh), 4.71 (d, *J* = 12.0 Hz, 1H, C*H*HNAP), 4.37 (d, *J* = 10.8 Hz, 1H, C*H*HPh), 4.18−4.10 (m, 3H, H-5, H-6a, H-6b), 3.96−3.91 (dd, *J* = 9.0, 2.9 Hz, 1H, H-3), 3.81 (dd, *J* = 3.0, 1.9 Hz, 1H, H-2), 3.72 (t, *J* = 9.3 Hz, 1H, H-4), 2.26 (s, 3H, CH_3Ts), 0.83 (s, 9H, C(CH_3)$_3$), 0.01 (s, 6H, 2 × CH_3Si); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.6−133.1 (7 × C-Ar), 131.8−125.8 (*C*H-Ar), 86.3 (C-1), 80.8 (C-2), 75.4 (C-4); 75.2 (*C*H_2Ph), 73.8 (C-3), 73.1 (*C*H_2NAP), 71.3 (C-5), 68.9 (C-6), 26.1 (C(*C*H_3)$_3$), 21.7 (*C*H_3Ts), 18.2 (*C*(CH$_3$)$_3$), −4.2 (*C*H_3Si), −4.5 (*C*H_3Si); MS (ESI-TOF) *m*/*z* 788.9 $[M + NH_4]^+$, *m*/*z* 793.8 $[M + Na]^+$; HRMS (ESI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{43}H_{51}O_7S_2Si$, 771.2840; found, 771.2842.

Phenyl 3-*O*-Allyl-4-*O*-benzyl-2-*O*-(2-naphthylmethyl)-1-thio-6-*O*-tosyl-α-D-mannopyranoside (16). To a cooled solution (0 °C) of a mixture of alcohols **11** and **13** (9.13 g, 16.8 mmol, 1.0 equiv) in anhydrous py (84.1 mL) were added TsCl (9.62 g, 50.5 mmol, 3.0 equiv) and DMAP (206 mg, 1.68 mmol, 0.1 equiv) under Ar. The mixture was stirred for 18 h at rt, quenched with MeOH (25 mL), and diluted with EtOAc (300 mL). The organic phase was washed with a 10% HCl(aq) solution (3 × 100 mL), a saturated $NaHCO_3$(aq) solution (100 mL), and brine (100 mL). Solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 10:0 to 6:4) to give **16** (10.3 g, 88%) as a yellow oil: R_f 0.5 (PE/EtOAc 8:2); $[\alpha]_D^{20}$ = +24.7 (*c* 0.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84−7.17 (m, 21H, C*H*-Ar), 5.95−5.85 (m, 1H, H-2All), 5.47 (d, *J* = 1.5 Hz, 1H, H-1), 5.31 (ddd, *J* = 17.3, 4.8, 1.6 Hz, 1H, H-3aAll), 5.20 (ddd, *J* = 10.3, 4.1, 1.5 Hz, 1H, H-3bAll), 4.91 (d, *J* = 10.7 Hz, 1H, C*H*HPh), 4.87 (d, *J* = 12.5 Hz, 1H, C*H*HNAP), 4.80 (d, *J* = 12.5 Hz, 1H, C*H*HNAP), 4.49 (d, *J* = 10.7 Hz, 1H, C*H*HPh), 4.34−4.28 (m, 2H, H-6a, H-6b), 4.26−4.23 (m, 1H, H-5), 4.08−4.05 (m, 2H, H-1aAll, H-1bAll), 4.02 (dd, *J* = 3.1, 1.7 Hz, 1H, H-2), 3.92 (t, *J* = 9.5 Hz, 1H, H-4), 3.71 (dd, *J* = 9.4, 3.1 Hz, 1H, H-3), 2.35 (s, 3H, CH_3Ts); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2−131.7 (7 × C-Ar), 134.5 (C-2All), 129.8−125.9 (*C*H-Ar), 117.5 (C-3All), 85.9 (C-1), 79.9 (C-3), 76.1 (C-2), 75.3 (*C*H_2Ph), 74.1 (C-4), 72.3 (*C*H_2NAP), 71.2 (C-1All), 71.0 (C-5), 68.8 (C-6), 21.7 (*C*H_3Ts); MS (ESI-TOF) *m*/*z* 714.7 $[M + NH_4]^+$, *m*/*z* 719.6 $[M + Na]^+$; HRMS (ESI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{40}H_{41}O_7S_2$, 697.2288; found, 697.2281.

Phenyl 3-*O*-Allyl-4-*O*-benzyl-6-chloro-2-*O*-(2-naphthylmethyl)-1-thio-α-D-mannopyranoside (17). To a cooled solution (0 °C) of a mixture of alcohols **11** and **13** (0.51 g, 0.94 mmol, 1.0 equiv) in anhydrous py (5 mL) were added TsCl (0.54 g, 2.8 mmol, 3.0 equiv) and DMAP (12 mg, 0.1 mmol, 0.1 equiv) under N_2. The mixture was stirred for 20 h and gradually warmed to rt. Additional TsCl (0.38 g, 1.9 mmol, 2 equiv) was added, and the mixture was stirred at 60 °C for 16 h. Then, the reaction mixture was cooled to rt and diluted with EtOAc (20 mL). The organic phase was washed with a 10% HCl(aq) solution (10 mL), a saturated $NaHCO_3$(aq) solution (10 mL), and brine (10 mL). Solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 10:0 to 8:2) to provide **17** (118 mg, 22%) and **16** (141 mg, 21%) as yellow oils. Analytical data of **16**: R_f 0.9 (PE/EtOAc 8:2); $[\alpha]_D^{20}$ = +35.4 (*c* 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79−7.13 (m, 17H, C*H*-Ar), 5.91−5.79 (m, 1H, H-2All), 5.54 (d, *J* = 1.5 Hz, 1H, H-1), 5.26 (ddd, *J* = 17.3, 3.7, 1.6 Hz, 1H, H-3aAll), 5.14 (ddd, *J* = 10.4, 3.3, 1.5 Hz, 1H, H-3bAll), 4.93 (d, *J* = 10.8 Hz, 1H, C*H*HPh), 4.85 (d, *J* = 12.6 Hz, 1H, C*H*HNAP), 4.78 (d, *J* = 12.6 Hz, 1H, C*H*HNAP), 4.61 (d, *J* = 10.8 Hz, 1H, C*H*HPh), 4.27−4.23 (m, 1H, H-5), 4.07−3.95 (m, 4H, H-1aAll, H-1bAll, H-4, H-2), 3.76−3.74 (m, 2H, H-6a, H-6b), 3.70 (dd, *J* = 9.4, 3.0 Hz, 1H, H-3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.3−133.2 (5 × C-Ar), 134.6 (C-2All), 131.7−125.9 (*C*H-Ar), 117.5 (C-3All), 86.2 (C-1), 79.8 (C-3), 76.2 (C-2), 75.7 (C-4), 75.6 (*C*H_2Ph), 72.6 (C-5), 72.2 (*C*H_2NAP), 71.2 (C-1All), 44.8 (C-6); MS (ESI-TOF) *m*/*z* = 578.4 $[M + NH_4]^+$; HRMS (ESI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{33}H_{34}ClO_4S$, 561.1861; found, 561.1862.

Phenyl 4-*O*-Benzyl-3-*O*-*tert*-butyldimethylsilyl-6-cyano-2-*O*-(2-naphthylmethyl)-1-thio-α-D-mannopyranoside (18). Tosylated **15** (0.86 g, 1.1 mmol, 1.0 equiv) was dissolved in anhydrous CH_3CN (11 mL), and freshly activated 4 Å molecular sieves (0.8 g) were added. The suspension was stirred for 30 min at rt under N_2, and then KCN (0.36 g, 5.5 mmol, 5.0 equiv) and 18-crown-6 (588 mg, 2.22 mmol, 2.0 equiv) were added. The mixture was stirred for 24 h at ∼55 °C under N_2. The mixture was cooled to rt, diluted with EtOAc (100 mL), and filtered over Celite. The filtrate was washed with a 10% HCl(aq) solution (25 mL), a saturated $NaHCO_3$(aq) solution (25 mL), and water (25 mL). Solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 95:5) to furnish **18** (0.61 g, 88%) as a yellow oil: R_f 0.5 (PE/EtOAc 8:2); $[\alpha]_D^{20}$ = +99.6 (*c* 0.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86−7.22 (m, 17H, C*H*-Ar),

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5.46 (d, J = 1.6 Hz, 1H, H-1), 4.98 (d, J = 11.6 Hz, 1H, C*H*HPh), 4.93 (d, J = 11.9 Hz, 1H, C*H*HNAP), 4.83 (d, J = 11.9 Hz, 1H, C*H*HNAP), 4.61 (d, J = 11.6 Hz, 1H, C*H*HPh), 4.27 (ddd, J = 9.6, 6.8, 3.2 Hz, 1H, H-5), 4.07 (dd, J = 9.1, 2.9 Hz, H-3), 3.96 (dd, J = 2.8, 1.8 Hz, 1H, H-2), 3.82 (t, J = 9.3 Hz, 1H, H-4), 2.65 (dd, J = 16.8, 3.0 Hz, 1H, H-6a), 2.49 (dd, J = 16.9, 7.7 Hz, 1H, H-6b), 0.97 (s, 9H, C(CH_3)$_3$), 0.18 (s, 6H, 2 × CH_3Si); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.9−133.1 (5 × C-Ar), 131.9−125.3 (*C*H-Ar), 117.3 (*C*N), 86.7 (C-1), 80.9 (C-2), 78.2 (C-4), 75.6 (CH_2Ph), 73.8 (C-3), 73.2 (CH_2NAP), 69.1 (C-5), 26.1 (C(CH_3)$_3$), 20.9 (C-6), 18.2 (C(CH_3)$_3$), −4.1 (CH_3Si), −4.5 (CH_3Si); MS (ESI-TOF) m/z 643.8 [M + NH_4]$^+$, m/z 648.7 [M + Na]$^+$; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{37}H_{44}NO_4SSi$, 626.2755; found, 626.2756.

Phenyl 3-*O*-Allyl-4-*O*-benzyl-6-cyano-2-*O*-(2-naphthylmethyl)-1-thio-α-D-mannopyranoside (19). Tosylated **16** (0.97 g, 1.4 mmol, 1.0 equiv) was dissolved in anhydrous CH_3CN (13.9 mL), and freshly activated 4 Å molecular sieves (0.8 g) were added. The suspension was stirred for 30 min at rt under N_2, and then KCN (0.72 g, 11 mmol, 8.0 equiv) and 18-crown-6 (0.74 g, 2.8 mmol, 2.0 equiv) were added. The mixture was stirred at 80 °C for 1 h. The solution was cooled to rt, diluted with EtOAc (15 mL), and filtered over Celite. The filtrate was washed with a 10% HCl(aq) solution (10 mL), brine (10 mL), and water (10 mL). Solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 95:5 to 85:15) to furnish **19** (0.52 g, 67%) as a white crystalline solid: R_f 0.5 (PE/EtOAc 8:2); mp 113−116 °C (DCM); $[\alpha]_D^{20}$ = +57.3 (c 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89−7.29 (m, 17H, C*H*-Ar), 6.00−5.86 (m, 1H, H-2All), 5.52 (s, 1H, H-1), 5.34 (d, J = 17.5 Hz, 1H, H-3aAll), 5.23 (d, J = 10.6 Hz, 1H, H-3bAll), 5.02 (d, J = 11.1 Hz, 1H, C*H*HPh), 4.91 (d, J = 12.5 Hz, 1H, C*H*HNAP), 4.85 (d, J = 12.5 Hz, 1H, C*H*HNAP), 4.66 (d, J = 11.1 Hz, 1H, C*H*HPh), 4.29 (ddd, J = 9.5, 7.2, 3.1 Hz, 1H, H-5), 4.14−4.05 (m, 3H, H-1aAll, H-1bAll, H-2), 3.87 (t, J = 9.3 Hz, 1H, H-4), 3.75 (dd, J = 9.3, 2.9 Hz, 1H, H-3), 2.74 (dd, J = 16.8, 3.4 Hz, 1H, H-6a), 2.60 (dd, J = 16.9, 7.5 Hz, 1H, H-6b); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.1−133.2 (5 × C-Ar), 134.4 (C-2All), 131.8−125.9 (*C*H-Ar), 117.7 (C-3All), 86.4 (C-1), 79.8 (C-3), 77.4 (C-4), 76.2 (C-2), 75.6 (CH_2Ph), 72.4 (CH_2NAP), 71.1 (C-1All), 68.8 (C-5), 21.1 (C-6); MS (ESI-TOF) m/z 569.6 [M + NH_4]$^+$, m/z 574.6 [M + Na]$^+$; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{34}H_{34}NO_4S$, 552.2203; found, 552.2197.

Phenyl 4-*O*-Benzyl-3-*O*-*tert*-butyldimethylsilyl-6-deoxy-2-*O*-(2-naphthylmethyl)-1-thio-α-D-*manno*-heptopyranoside (20). To a solution of nitrile **18** (0.31 g, 500 μmol, 1.0 equiv) in anhydrous toluene (5 mL) was added dropwise DIBALH (1.0 M in toluene, 1.5 mL, 1.5 mmol, 3.0 equiv) at −78 °C under Ar. After being stirred for 15 min, the reaction mixture was diluted with EtOAc (30 mL), and the organic phase was washed with brine (15 mL) and dried over $MgSO_4$. The solutions were concentrated under reduced pressure. The crude imine was dissolved in a mixture of 1 N HCl(aq)/THF (1:9, 5 mL). After being stirred for 1 h at rt, the mixture was diluted with EtOAc (15 mL), and the organic phase was washed with brine (10 mL). The solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure. The crude aldehyde was dissolved in MeOH/DCM (2:1, 7.5 mL), and $NaBH_4$ (21 mg, 550 μmmol, 1.1 equiv) was added. The mixture was stirred at rt for 1 h under N_2. The reaction was quenched with acetone (10 mL) and diluted with DCM (20 mL), and the organic layer was washed with brine (2 × 15 mL). The solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 95:5 to 70:30) to give **20** (101 mg, 60%, three steps) as a yellow oil: R_f 0.1 (PE/Et_2O 7:3); $[\alpha]_D^{20}$ = +68.5 (c 0.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70−7.05 (m, 17H, C*H*-Ar), 5.30 (d, J = 1.7 Hz, 1H, H-1), 4.81 (d, J = 10.4 Hz, 1H, C*H*HNAP), 4.78 (d, J = 9.7 Hz, 1H, C*H*HPh), 4.68 (d, J = 11.9 Hz, C*H*HNAP), 4.45 (d, J = 11.3 Hz, 1H, C*H*HPh), 4.02 (td, J = 9.3, 2.8 Hz, 1H, H-5), 3.94 (dd, J = 9.0, 2.9 Hz, 1H, H-3), 3.78 (dd, J = 3.0, 1.8 Hz, 1H, H-2), 3.57 (t, J = 9.4 Hz, 1H, H-4), 3.48−3.44 (m, 2H, H-7), 1.93−1.86 (m, 1H, H-6a), 1.64−1.56 (m, 1H, H-6b), 0.83 (s, 9H, 3 × C(CH_3)$_3$), 0.00 (s, 3H, CH_3Si), −0.01 (s, 3H, CH_3Si); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4−133.2 (5 × C-Ar), 128.5−125.9 (*C*H-Ar), 86.5 (C-1), 80.9 (C-2), 79.4 (C-4), 75.5 (CH_2Ph), 73.8 (C-3), 73.5 (CH_2NAP), 72.8 (C-5), 60.9 (C-7), 33.8 (C-6), 26.1 (C(CH_3)$_3$Si), 18.2 (C(CH_3)$_3$Si), −4.2 (CH_3Si), −4.5 (CH_3Si); HRMS (ESI-TOF) m/z [M + NH_4]$^+$ calcd for $C_{37}H_{50}NO_5SSi$, 648.3173; found, 648.3177.

Phenyl 3-*O*-Allyl-4-*O*-benzyl-6-deoxy-2-*O*-(2-naphthylmethyl)-1-thio-D-*manno*-heptopyranoside (21). To a solution of nitrile **19** (1.2 g, 2.1 mmol, 1.0 equiv) in anhydrous toluene (21 mL) was added dropwise DIBALH (1.0 M in toluene, 2.5 mL, 2.5 mmol, 1.2 equiv) −78 °C under Ar. The mixture was stirred for 25 min and gradually warmed to −35 °C. The mixture was diluted with EtOAc (20 mL), and the organic phase was washed with a 10% HCl(aq) solution (3 × 10 mL), a saturated $NaHCO_3$(aq) solution (10 mL), and brine (10 mL). The solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure. The crude imine was dissolved in a mixture of 1 N HCl(aq)/THF (1:9, 21 mL) and stirred for 1 h at rt. The mixture was diluted with EtOAc (25 mL), and the organic phase was washed with water (2 × 10 mL) and brine (10 mL). The solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure. Crude aldehyde was dissolved in MeOH/DCM (2:1, 32 mL), and $NaBH_4$ (88 mg, 2.3 mmol, 1.1 equiv) was added. The mixture was stirred at rt for 20 min under N_2. The reaction mixture was quenched with acetone (10 mL) and diluted with DCM (20 mL). The organic layer was washed with water (10 mL) and brine (10 mL). The solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 9:1 to 7:3) to give **21** (1.02 g, 87%, three steps) as a white amorphous solid: R_f 0.3 (PE/EtOAc 8:2); $[\alpha]_D^{20}$ = +57.9 (c 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81−7.14 (m, 17H, C*H*-Ar), 5.94−5.81 (m, 1H, H-2All), 5.45 (d, J = 1.0 Hz, 1H, H-1), 5.26 (dd, J = 17.5, 1.5 Hz, 1H, H-3aAll), 5.14 (dd, J = 10.5, 1.2 Hz, 1H, H-3bAll), 4.91 (d, J = 10.8 Hz, 1H, C*H*HPh), 4.83 (s, 2H, CH_2NAP), 4.56 (d, J = 10.8 Hz, 1H, C*H*HPh), 4.16−4.07 (m, 1H, H-5), 4.04−4.03 (m, 2H, H-1aAll, H-1bAll), 3.99 (br s, 1H, H-2), 3.71−3.69 (m, 2H, H-4, H-3), 3.58−3.55 (m, 2H, H-7a, H-7b), 2.09−2.02 (m, 1H, H-6a), 1.79−1.70 (m, 1H, H-6b); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.1−133.2 (5 × C-Ar), 134.7 (C-2All), 131.8−126.1 (*C*H-Ar), 117.4 (C-3All), 85.9 (C-1), 79.9 (C-3), 78.5 (C-4), 76.2 (C-2), 75.6 (CH_2Ph), 72.6 (CH_2NAP), 72.4 (C-5), 71.2 (C-1All), 60.8 (C-7), 34.1 (C-6); MS (ESI-TOF) m/z = 579.6 [M + Na]$^+$; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{34}H_{37}O_5S$, 557.2356; found, 557.2347.

Phenyl 4,7-Di-*O*-benzyl-3-*O*-*tert*-butyldimethylsilyl-6-deoxy-2-*O*-(2-naphthylmethyl)-1-thio-α-D-*manno*-heptopyranoside (23). To a cooled (0 °C) solution of alcohol **20** (191 mg, 303 μmol, 1.0 equiv) in anhydrous DMF (1.2 mL) was slowly added NaH (60% oil dispersion, 36 mg, 910 μmol, 3.0 equiv) under N_2. The mixture was stirred for 30 min at this temperature. BnBr (72 μL, 610 μmol) was then added dropwise, and the mixture was gradually warmed to rt. After being stirred for 20 h, the reaction was quenched with MeOH (4 mL) and diluted with EtOAc (25 mL). The organic layer was washed with water (2 × 15 mL), and the solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (pentane/Et_2O 95:5 to 90:10) to give **23** (110 mg, 50%) as a yellow oil: R_f 0.7 (PE/EtOAc 8:2); $[\alpha]_D^{20}$ = +72.3 (c 0.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71−7.02 (m, 22H, C*H*-Ar), 5.37 (d, J = 1.6 Hz, 1H, H-1), 4.81 (d, J = 11.8 Hz, 1H, C*H*HNAP), 4.78 (d, J = 11.2 Hz, 1H, C*H*HPh), 4.71 (d, J = 11.9 Hz, C*H*HNAP), 4.49 (d, J = 11.3 Hz, 1H, C*H*HPh), 4.23 (s, 2H, CH_2Ph), 4.01 (td, J = 9.5, 2.3 Hz, 1H, H-5), 3.94 (dd, J = 9.0, 2.9 Hz, 1H, H-3), 3.80 (dd, J = 3.0, 1.8 Hz, 1H, H-2), 3.56 (t, J = 9.3 Hz, 1H, H-4), 3.37−3.28 (m, 2H, H-7), 2.11−2.04 (m, 1H, H-6a), 1.71−1.63 (m, 1H, H-6b), 0.83 (s, 9H, C(CH_3)$_3$), 0.00 (s, 3H, CH_3Si), −0,01 (s, 3H, CH_3Si); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7−133.4 (6 × C-Ar), 131.4−126.0 (*C*H-Ar), 86.2 (C-1), 81.0 (C-2), 79.8 (C-4), 75.3 (CH_2Ph), 74.0 (C-3), 73.4 (CH_2NAP), 72.9 (CH_2Ph), 70.5 (C-5), 67.1 (C-7), 31.8 (C-6), 26.1 (C(CH_3)$_3$), 18.2 (C(CH_3)$_3$), −4.2 (CH_3Si), −4.5 (CH_3Si); MS (ESI-TOF) m/z = 579.6 [M + Na]$^+$; HRMS (ESI-TOF) m/z [M + NH_4]$^+$ calcd for $C_{44}H_{56}NO_5SSi$, 738.3643; found, 738.3644.

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Phenyl 3-*O*-Allyl-4,7-di-*O*-benzyl-6-deoxy-2-*O*-(2-naphthylmethyl)-1-thio-α-D-*manno*-heptopyranoside (25). To a cooled (0 °C, ice water/water bath) solution of alcohol **21** (1.03 g, 1.84 mmol, 1.0 equiv) in anhydrous DMF (7.4 mL) was slowly added NaH (60% oil dispersion, 0.37 g, 9.2 mmol, 4.0 equiv) under Ar. The mixture was stirred for 30 min at this temperature. Then, TBAI (100 mg, 0.28 mmol, 0.15 equiv) followed by BnBr (0.66 mL, 5.5 mmol, 3.0 equiv) was added, and the mixture was gradually warmed to rt. After being stirred for 7 h, the reaction was quenched with MeOH (8 mL) and diluted with EtOAc (25 mL). The organic layer was washed with water (3 × 15 mL) and brine (15 mL), and the solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (PE/EtOAc 10:0 to 9:1) to give **25** (1.2 g, 97%) as a yellow oil: R_f 0.7 (PE/EtOAc 8:2); $[\alpha]_D^{20}$ = +34.6 (*c* 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85−7.16 (m, 22H, C*H*-Ar), 5.99−5.86 (m, 1H, H-2All), 5.56 (d, *J* = 1.2 Hz, 1H, H-1), 5.32 (dd, *J* = 17.1, 1.6 Hz, 1H, H-3aAll), 5.19 (dd, *J* = 10.5, 1.4 Hz, 1H, H-3bAll), 4.96 (d, *J* = 10.6 Hz, 1H, C*H*HPh), 4.92 (d, *J* = 12.5 Hz, 1H, C*H*HNAP), 4.87 (d, *J* = 12.5 Hz, 1H, C*H*HNAP), 4.65 (d, *J* = 10.6 Hz, 1H, C*H*HPh), 4.38 (s, 2H, CH_2Ph), 4.17−4.13 (m, 1H, H-5), 4.09 (d, *J* = 5.4 Hz, 2H, H-1aAll, H-1bAll), 4.05 (s, 1H, H-2), 3.76−3.74 (m, 2H, H-3, H-4), 3.53−3.41 (m, 2H, H-7a, H-7b), 2.31−2.24 (m, 1H, H-6a), 1.91−1.82 (m, 1H, H−6b); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7−133.2 (6 × C-Ar), 134.8 (C-2All), 131.4−126.1 (*C*H-Ar), 117.3 (C-3All), 85.7 (C-1), 80.1 (C-3), 78.9 (C-4), 76.4 (C-2), 75.5 (CH_2Ph−C4), 73.0 (CH_2Ph−C7), 72.5 (CH_2NAP), 71.3 (C-1All), 70.3 (C-5), 67.1 (C-7), 32.0 (C-6); MS (ESI-TOF) *m*/*z* = 669.7 $[M + Na]^+$; HRMS (ESI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{41}H_{43}O_5S$, 647.2826; found, 647.2815.

(5-Azido-1-pentyl) 3-*O*-Allyl-4,7-di-*O*-benzyl-6-deoxy-2-*O*-(2-naphthylmethyl)-α-D-*manno*-heptopyranoside (27) and (5-Azido-1-pentyl) 3-*O*-Allyl-4,7-di-*O*-benzyl-6-deoxy-2-*O*-(2-naphthylmethyl)-β-D-*manno*-heptopyranoside (28). *Representative Procedure for Intermolecular Glycosylation without Donor Preactivation.* To a solution of donor **25** (20 mg, 31 μmol, 1.0 equiv) and 5-azido-1-pentanol[66] (**26**, 8.0 mg, 62 μmol, 2.0 equiv) in anhydrous CH_3CN (620 μL) were added freshly activated 4 Å powdered molecular sieves (80 mg) and DTBMP (19 mg, 93 μmol, 3.0 equiv). The mixture was stirred for 40 min at rt under Ar. Then, Me_2S_2 (8.4 μL, 93 μmol, 3.0 equiv) followed by MeOTf (10.5 μL, 93 μmol, 3.0 equiv) was added at −10 °C. The mixture was stirred for 5 h and gradually warmed to rt. The reaction was quenched with Et_3N (500 μL), filtered over Celite, and rinsed with DCM. The filtrate was concentrated under reduced pressure and purified by silica gel flash chromatography (PE/EtOAc 10:0 to 7:3) to give **27** (8.8 mg, 42%) and **28** (10 mg, 48%) as yellow oils. Analytical data for **27**: R_f 0.30 (PE/EtOAc 9:1); $[\alpha]_D^{20}$ = +24.2 (*c* 0.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84−7.26 (m, 17H, C*H*-Ar), 6.10−5.91 (m, 1H, H-2All), 5.33 (dd, *J* = 17.3, 1.4 Hz, 1H, H-3aAll), 5.18 (dd, *J* = 10.5, 1.1 Hz, 1H, H-3bAll), 4.95 (d, *J* = 10.7 Hz, 1H, C*H*HPh), 4.96 (d, *J* = 12.5 Hz, 1H, C*H*HPh), 4.89 (d, *J* = 12.5 Hz, 1H, C*H*HPh), 4.74 (s, 1H, H-1), 4.65 (d, *J* = 10.6 Hz, 1H, C*H*HPh), 4.50 (d, *J* = 11.9 Hz, 1H, C*H*HNAP), 4.45 (d, *J* = 11.9 Hz, 1H, C*H*HNAP), 4.13−4.11 (m, 2H, H-1aAll, H-1bAll), 3.77−3.74 (m, 2H, H-2, H-3), 3.71−3.69 (m, 2H, H-5, H-4), 3.67−3.62 (m, 2H, H-7a, H-7b), 3.54 (dt, *J* = 9.6, 6.7 Hz, 1H, H-1a$_{linker}$), 3.24 (dt, *J* = 9.6, 6.3 Hz, 1H, H-1b$_{linker}$), 3.11 (t, *J* = 6.7 Hz, 2H, H-5$_{linker}$), 2.32−2.25 (m, 1H, H-6a), 1.84−1.76 (m, 1H, H-6b), 1.49−1.39 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.24−1.20 (m, 2H, H-3$_{linker}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7−133.2 (5 × C-Ar), 135.1 (C-2All), 128.5−126.1 (*C*H-Ar), 116.7 (C-3All), 98.0 (C-1, $^1J_{C,H}$ = 168 Hz), 80.3 (C-3), 79.1 (C-4), 75.5 (CH_2Ph), 74.8 (C-2), 73.1 (CH_2Ph), 72.9 (CH_2NAP), 71.3 (C-1All), 68.5 (C-5), 67.0 (C-7), 66.9 (C-1$_{linker}$), 51.3 (C-5$_{linker}$), 31.9 (C-6), 29.0 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 23.5 (C-3$_{linker}$); MS (ESI-TOF) *m*/*z* = 688.7 $[M + Na]^+$; HRMS (ESI-TOF) *m*/*z* $[M + NH_4]^+$ calcd for $C_{40}H_{51}N_4O_6$, 683.3803; found, 683.3799. Analytical data for **28**: R_f 0.26 (PE/EtOAc 9:1); $[\alpha]_D^{20}$ = −19.2 (*c* 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87−7.27 (m, 17H, C*H*-Ar), 5.90−5.80 (m, 1H, H-2All), 5.25 (ddd, *J* = 17.2, 4.0, 1.7 Hz, 1H, H-3aAll), 5.13 (dd, *J* = 10.4, 1.5 Hz, 1H, H-3bAll), 5.11 (d, *J* = 12.8 Hz, 1H, C*H*HPh), 5.03 (d, *J* = 12.8 Hz, 1H, C*H*HPh), 4.95 (d, *J* = 10.7 Hz, 1H, C*H*HPh), 4.64 (d, *J* = 10.7 Hz, 1H, C*H*HPh), 4.53 (d, *J* = 12.1 Hz, 1H, C*H*HNAP), 4.43 (d, *J* = 12.1 Hz, 1H, C*H*HNAP), 4.29 (s, 1H, H-1), 3.98 (ddt, *J* = 12.7, 5.3, 1.4 Hz, 1H, H-1aAll), 3.92 (ddt, *J* = 12.8, 5.4, 1.3 Hz, 1H, H-1bAll), 3.88 (d, *J* = 2.8 Hz, 1H, H-2), 3.84 (dt, *J* = 9.4, 6.2 Hz, 1H, H-1a$_{linker}$), 3.71−3.60 (m, 3H, H-7ab, H-4), 3.39−3.29 (m, 3H, H-3, H-5, H-1b$_{linker}$), 3.23 (td, *J* = 6.9, 1.5 Hz, 2H, H-5$_{linker}$), 2.34−2.25 (m, 1H, H-6a), 1.88−1.80 (m, 1H, H-6b), 1.67−1.57 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.47−1.41 (m, 2H, H-3$_{linker}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7−133.2 (5 × C-Ar), 134.7 (C-2All), 128.3−125.7 (*C*H-Ar), 116.8 (C-3All), 101.5 (C-1, $^1J_{C,H}$ = 154 Hz), 82.5 (C-3), 78.5 (C-4), 75.4 (CH_2Ph), 74.1 (CH_2Ph), 73.8 (C-2), 72.9 (CH_2NAP), 72.3 (C-5), 70.7 (C-1All), 69.4 (C-1$_{linker}$), 66.6 (C-7), 51.4 (C-5$_{linker}$), 31.9 (C-6), 29.3 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 23.5 (C-3$_{linker}$); HRMS (ESI-TOF) *m*/*z* $[M + NH_4]^+$ calcd for $C_{40}H_{51}N_4O_6$, 683.3803; found, 683.3803.

Methyl 3-*O*-Allyl-4,7-di-*O*-benzyl-6-deoxy-2-*O*-(2-naphthylmethyl)-1-thio-α-D-*manno*-heptopyranoside (29). To a solution of glycosyl donor **25** (20 mg, 31 μmol, 1.0 equiv), Me_2S_2 (8.4 μL, 93 μmol, 3.0 equiv), and DTBMP (19 mg, 93 μmol, 3.0 equiv) in anhydrous DCM (310 μL) was added freshly activated 4 Å powdered molecular sieves (80 mg). The mixture was stirred for 50 min at rt under Ar. Then, the reaction mixture was cooled to −78 °C, and Tf_2O (15.6 μL, 93 μmol, 3.0 equiv) was added dropwise. The mixture was stirred for 15 min at −78 °C before acceptor **26** (8.0 mg, 62 μmol, 2.0 equiv) in anhydrous DCM (150 μL) was added dropwise. The reaction mixture was stirred at −78 °C for 2 h and then gradually warmed to −30 °C. The reaction was quenched with Et_3N (500 μL), filtered over Celite, and rinsed with DCM. The filtrate was concentrated under reduced pressure and purified by silica gel flash chromatography (PE/Et_2O 100:0 to 95:5) to give **29** (7.2 mg, 18%) as a yellow oil: R_f 0.5 (PE/EtOAc 8:2); $[\alpha]_D^{20}$ = +20.6 (*c* 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84−7.25 (m, 17H, C*H*-Ar), 5.95−5.85 (m, 1H, H-2All), 5.30 (dd, *J* = 17.3, 1.2 Hz, 1H, H-3aAll), 5.22 (s, 1H, H-1), 5.17 (dd, *J* = 10.5, 1.0 Hz, 1H, H-3bAll), 4.93 (d, *J* = 12.7 Hz, 1H, C*H*HNAP), 4.94 (d, *J* = 10.8 Hz, 1H, C*H*HPh), 4.86 (d, *J* = 12.7 Hz, 1H, C*H*HNAP), 4.63 (d, *J* = 10.8 Hz, 1H, C*H*HPh), 4.50 (d, *J* = 11.9 Hz, 1H, C*H*HPh), 4.46 (d, *J* = 11.9 Hz, 1H, C*H*HPh), 4.09−4.05 (m, 3H, H-5, H-1aAll, H-1bAll), 3.89 (br s, 1H, H-2), 3.75 (dd, *J* = 8.5, 2.8 Hz, 1H, H-3), 3.71 (t, *J* = 9.2 Hz, 1H, H-4), 3.62 (dd, *J* = 8.0, 5.7 Hz, 2H, H-7a, H-7b), 2.32−2.25 (m, 1H, H-6a), 2.01 (s, 3H, SCH_3), 1.90−1.81 (m, 1H, H-6b); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7−133.2 (5 × C-Ar), 134.9 (C-2All), 128.4−126.1 (*C*H-Ar), 117.1 (C-3All), 83.4 (C-1), 80.3 (C-3), 79.1 (C-4), 76.3 (C-2), 75.4 (CH_2Ph), 72.9 (CH_2Ph), 72.5 (CH_2NAP), 71.3 (C-1All), 69.1 (C-5), 67.1 (C-7), 32.0 (C-6), 13.7 (SCH_3); HRMS (ESI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{36}H_{41}O_5S$, 585.2669; found, 585.2664.

(5-Azido-1-pentyl) 4,7-Di-*O*-benzyl-6-deoxy-2-*O*-(2-naphthylmethyl)-β-D-*manno*-heptopyranoside (32). 1,5-Cyclooctadiene-bis(methyldiphenylphosphine)-iridium hexafluorophosphate (2.9 mg, 3.0 μmol, 0.1 equiv) was dissolved in anhydrous THF (700 μL), and the resulting red solution was degassed under Ar. Hydrogen was bubbled through the solution for 5 min, and then the resulting yellow solution was once again degassed under Ar. A solution of heptoside **28** (23 mg, 34 μmol, 1.0 equiv) in anhydrous THF (700 μL) was added. The mixture was stirred for 1 h at rt under Ar. Then, a solution of iodine (17.4 mg, 69 μmol, 2.0 equiv) in THF/H_2O (1 mL, 4:1 v/v) was added to the mixture, which was stirred for another 1 h at rt. The excess of iodine was then quenched by adding a freshly prepared 10% $Na_2S_2O_3$(aq) solution. The aqueous phase was extracted with EtOAc (3 × 5 mL). The combined organic layers were washed with a saturated $NaHCO_3$(aq) solution (10 mL) and brine (10 mL). The solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography (pentane/Et_2O 8:2 to 6:4) to afford **32** (20.7 mg, 97%, two steps) as a colorless oil: R_f 0.30 (PE/EtOAc 8:2); $[\alpha]_D^{20}$ = −28.8 (*c* 0.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86−7.24 (m, 17H, C*H*-Ar), 5.20 (d, *J* = 12.1 Hz, 1H, C*H*HNAP), 4.89 (d, *J* = 10.9 Hz, 1H, C*H*HPh), 4.80 (d, *J* = 12.1 Hz, 1H, C*H*HNAP), 4.62 (d, *J* = 10.9 Hz, 1H, C*H*HPh), 4.54 (d, *J* = 12.0 Hz, 1H, C*H*HPh), 4.44 (d, *J* = 12.0 Hz, 1H, C*H*HPh), 4.41 (s, 1H, H-1), 3.87−3.82 (m, 2H, H-

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1a$_{linker}$, H-2), 3.70−3.60 (m, 3H, H-7ab, H-4), 3.41−3.33 (m, 3H, H-1b$_{linker}$, H-3, H-5), 3.25 (t, J = 6.8 Hz, 2H, H-5$_{linker}$), 2.33−2.26 (m, 1H, H-6a), 1.87−1.77 (m, 1H, H-6b), 1.71−1.58 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.49−1.42 (m, 2H, H-3$_{linker}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5−133.2 (5 × C-Ar), 128.5−126.1 (*C*H-Ar), 101.8 (C-1), 80.7 (C-3), 78.1 (C-2), 75.3 (*C*H$_2$NAP), 75.0 (*C*H$_2$Ph), 74.4 (C-4), 72.9 (*C*H$_2$Ph), 72.0 (C-5), 69.6 (C-1$_{linker}$), 66.5 (C-7), 51.4 (C-5$_{linker}$), 32.1 (C-6), 29.4 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 23.6 (C-3$_{linker}$); HRMS (ESI-TOF) m/z [M + NH_4]$^+$ calcd for $C_{37}H_{47}N_4O_6$, 643.3489; found, 643.3490.

General Procedure for the Synthesis of Mixed Acetals 33−39. To a mixture of donor **23** or **25** (1.0 equiv) and alcohol acceptor (1.2−1.5 equiv) in anhydrous DCM (20 mL·mmol^{-1}) was added freshly activated 4 Å powdered molecular sieves (4 mg·mg^{-1} of donor). The mixture was stirred at rt for 40 min under Ar. Then, DDQ (1.2 equiv) was added, and the deep-green mixture was stirred for 3 h at rt under Ar. The reaction was quenched by adding a saturated $NaHCO_3$(aq) solution, stirred until the color turned bright yellow (∼10 min), and diluted with DCM. The mixture was filtered over Celite and rinsed with DCM, and the organic phase was washed with a saturated $NaHCO_3$(aq) and brine. The solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure. The residue was purified by silica gel flash chromatography to give mixed acetals.

2-Naphthaldehyde(5-amino-*N*-benzyloxycarbonyl-1-pentyl)(phenyl 4,7-di-*O*-benzyl-3-*O*-*tert*-butyldimethylsilyl-6-deoxy-1-thio-α-D-*manno*-heptopyranosid-2-yl) Acetal (33). According to the general procedure for the synthesis of mixed acetals, donor **23** (104 mg, 150 μmol) was reacted with acceptor **40**[76] (70 mg, 210 μmol, 1.5 equiv) in the presence of DDQ (40 mg, 170 μmol, 1.2 equiv). Purification by silica gel flash chromatography (pentane/Et_2O 95:5 to 75:25) gave **33** (88 mg, 64%) as a yellow oil: R_f 0.7 (PE/EtOAc 7:3); HRMS (ESI-TOF) m/z [M + NH_4]$^+$ calcd for $C_{57}H_{73}N_2O_8SSi$, 973.4851; found, 973.4846. The mixed acetals were unstable and decomposed in the NMR tube ($CDCl_3$ or py-d_5).

2-Naphthaldehyde(5-amino-*N*-benzyloxycarbonyl-1-pentyl)(phenyl 3-*O*-allyl-4,7-di-*O*-benzyl-6-deoxy-1-thio-α-D-*manno*-heptopyranosid-2-yl) Acetal (34). According to the general procedure for the synthesis of mixed acetals, donor **25** (16 mg, 24 μmol) was reacted with acceptor **40**[76] (7 mg, 29 μmol, 1.2 equiv) in the presence of DDQ (7 mg, 29 μmol, 1.2 equiv). Purification by silica gel flash chromatography (PE/EtOAc 95:5 to 7:3 + 5% Et_3N) gave **34** (13.2 mg, 62%) as a yellow oil: R_f 0.2 (PE/Et_2O 7:3); $[\alpha]_D^{20}$ = +61.3 (c 0.2, $CHCl_3$); HRMS (ESI-TOF) m/z [M + NH_4]$^+$ calcd for $C_{54}H_{63}N_2O_8S$, 899.4300; found, 899.4294. The mixed acetals were unstable and decomposed in the NMR tube ($CDCl_3$ or py-d_5).

2-Naphthaldehyde(5-azido-1-pentyl)(phenyl 3-*O*-allyl-4,7-di-*O*-benzyl-6-deoxy-1-thio-α-D-*manno*-heptopyranosid-2-yl) Acetal (35). According to the general procedure for the synthesis of mixed acetals, donor **25** (20 mg, 32 μmol) was reacted with acceptor **26**[66] (5.3 mg, 41 μmol, 1.3 equiv) in the presence of DDQ (8.6 mg, 38 μmol, 1.2 equiv). Purification by silica gel flash chromatography (PE/Et_2O 95:5 to 7:3 + 5% Et_3N) gave **35** (20.2 mg, 81%) as a yellow oil: R_f 0.4 (PE/Et_2O 7:3); $[\alpha]_D^{20}$ = +72.7 (c 0.3, $CHCl_3$); ^{1}H NMR (400 MHz, py-d_5) δ 8.38−7.23 (m, 22H, C*H*-Ar), 6.24 (s, 1H, H-acetal), 6.07−5.96 (m, 1H, H-2All), 6.03 (d, J = 1.5 Hz, 1H, H-1), 5.42 (ddd, J = 17.3, 4.1, 1.7 Hz, 1H, H-3aAll), 5.17 (dd, J = 10.4, 1.6 Hz, 1H, H-3bAll), 5.12 (d, J = 11.2 Hz, 1H, C*H*HPh), 4.87 (s, 1H, H-2), 4.78 (d, J = 11.2 Hz, 1H, C*H*HPh), 4.63−4.57 (m, 1H, H-5), 4.44 (d, J = 11.9 Hz, 1H, C*H*HPh), 4.40 (d, J = 11.9 Hz, 1H, C*H*HPh), 4.34 (ddt, J = 13.0, 5.3, 1.4 Hz, 1H, H-1aAll), 4.24 (ddt, J = 13.2, 5.4, 1.5 Hz, 1H, H-1bAll), 4.08 (d, J = 2.3 Hz, 1H, H-3), 4.07 (d, J = 2.2 Hz, 1H, H-4), 3.76−3.60 (m, 4H, H-7ab, H-1ab$_{linker}$), 3.10 (t, J = 6.6 Hz, 1H, H-5$_{linker}$), 2.52−2.45 (m, 1H, H-6a), 2.02−1.94 (m, 1H, H-6b), 1.59−1.52 (m, 2H, H-2$_{linker}$), 1.49−1.35 (m, 4H, H-4$_{linker}$, H-3$_{linker}$); ^{13}C NMR (100 MHz, py-d_5) δ 139.8−133.9 (6 × C-Ar), 135.9 (C-2All), 132.4−124.2 (*C*HAr), 117.1 (C-3All), 104.1 (*C*H-acetal), 88.3 (C-1), 80.9 (C-3), 79.6 (C-4), 75.9 (C-2), 75.6 (*C*H$_2$Ph), 73.4 (*C*H$_2$Ph), 71.4 (C-1All), 70.7 (C-5), 67.4 (C-7), 65.9 (C-1$_{linker}$), 51.7 (C-5$_{linker}$), 32.8 (C-6), 29.9 (C-2$_{linker}$), 29.2 (C-4$_{linker}$), 24.1 (C-3$_{linker}$); MS (ESI-TOF) m/z = 796.7 [M + Na]$^+$; HRMS (ESI-TOF) m/z [M + NH_4]$^+$ calcd for $C_{46}H_{55}N_4O_6S$, 791.3837; found, 791.3832.

2-Naphthaldehyde(1,2:3,4-di-*O*-isopropylidene-α-D-galacto-pyranos-6-yl)(phenyl 3-*O*-allyl-4,7-di-*O*-benzyl-6-deoxy-1-thio-α-D-*manno*-heptopyranosid-2-yl) Acetal (36). According to the general procedure for the synthesis of mixed acetals, donor **25** (20.4 mg, 0.031 mmol) was reacted with acceptor **41** (9 mg, 34 μmol, 1.1 equiv) in the presence of DDQ (8.4 mg, 37 μmol, 1.2 equiv). Purification by silica gel flash chromatography (PE/EtOAc 9:1 to 8:2 + 5% Et_3N) gave **36** (17.4 mg, 62%) as a yellow oil: R_f 0.2 (PE/EtOAc 8:2); $[\alpha]_D^{20}$ = +42.9 (c 0.2, $CHCl_3$); ^{1}H NMR (400 MHz, py-d_5) δ 8.42−7.42 (m, 22H, C*H*-Ar), 6.43 (s, 1H, H-acetal), 6.37 (s, 1H, H-1$_A$), 6.07−5.98 (m, 1H, H-2All), 5.66 (d, J = 4.7 Hz, 1H, H-1$_B$), 5.42 (d, J = 17.4 Hz, 1H, H-3aAll), 5.17 (d, J = 10.8 Hz, 1H, H-3bAll), 5.10 (d, J = 11.1 Hz, 1H, C*H*HPh), 5.03 (s, 1H, H-2$_A$), 4.79 (s, 1H, H-3$_B$), 4.78 (d, J = 10.5 Hz, 1H, C*H*HPh), 4.61 (t, J = 7.7 Hz, 1H, H-5$_A$), 4.52 (br s, 1H, H-2$_B$), 4.46−4.37 (m, 4H, H-5$_B$, H-4$_B$, C*H*$_2$Ph), 4.30 (dd, J = 13.1, 5.1 Hz, 1H, H-1aAll), 4.26−4.19 (m, 2H, H-6a$_B$, H-1bAll), 4.16−4.09 (m, 2H, H-3$_A$, H-4$_A$), 3.94 (dd, J = 10.3, 3.9 Hz, 1H, H-6b$_B$), 3.64 (t, J = 6.2 Hz, 2H, H-7ab$_A$), 2.52−2.45 (m, 1H, H-6a$_A$), 2.03−1.94 (m, 1H, H-6b$_A$), 1.56 (s, 3H, C*H*$_3$), 1.49 (s, 3H, C*H*$_3$), 1.36 (s, 3H, C*H*$_3$), 1.31 (s, 3H, C*H*$_3$); ^{13}C NMR (100 MHz, py-d_5) δ 139.8−133.9 (6 × C-Ar), 135.8 (C-2All), 131.8−124.2 (*C*H-Ar), 117.2 (C-3All), 109.7 (C-iso), 109.0 (C-iso) 103.8 (*C*H-acetal), 97.2 (C-1$_B$), 87.6 (C-1$_A$), 81.2 (C-3$_A$), 79.6 (C-4$_A$), 75.7 (C-2$_A$), 75.6 (*C*H2Ph), 73.3 (*C*H2Ph), 72.2 (C-4$_B$), 71.6 (C-3$_B$), 71.3 (C-2$_B$), 71.2 (C-1All), 70.5 (C-5$_A$), 68.3 (C-5$_B$), 67.4 (C-7$_A$), 64.3 (C-6$_B$), 32.7 (C-6$_A$), 26.7−24.9 (4 × CH_3); HRMS (ESI-TOF) m/z [M + NH_4]$^+$ calcd for $C_{53}H_{64}NO_{11}S$, 922.4195; found, 922.4191.

2-Naphthaldehyde(1,2:5,6-di-*O*-isopropylidene-α-D-gluco-furanos-3-yl)(phenyl 3-*O*-allyl-4,7-di-*O*-benzyl-6-deoxy-1-thio-α-D-*manno*-heptopyranosid-2-yl) Acetal (37). According to the general procedure for the synthesis of mixed acetals, donor **25** (15 mg, 23 μmol) was reacted with acceptor **42** (9.1 mg, 35 μmol, 1.5 equiv) in the presence of DDQ (6.3 mg, 28 μmol, 1.2 equiv). Purification by silica gel flash chromatography (PE/EtOAc 95:5 to 80:20 + 5% Et_3N) gave **37** (17.2 mg, 83%) as a yellow amorphous solid: R_f 0.6 (PE/EtOAc 8:2); $[\alpha]_D^{20}$ = +41.5 (c 0.3, $CHCl_3$); ^{1}H NMR (400 MHz, py-d_5) δ 8.40−7.24 (m, 22H, C*H*-Ar), 6.42 (s, 1H, H-acetal), 6.20 (s, 1H, H-1$_A$), 6.14 (d, J = 3.5 Hz, 1H, H-1$_B$), 6.14−6.05 (m, 1H, H-2All), 5.49 (dd, J = 17.2, 1.4 Hz, 1H, H-3aAll), 5.26 (dd, J = 10.6, 1.0 Hz, 1H, H-3bAll), 5.08−5.07 (m, 2H, H-2$_A$, C*H*HPh), 4.90 (dd, J = 14.3, 6.2 Hz, 1H, H-5$_B$), 4.79 (d, J = 3.6 Hz, 1H, H-2$_B$), 4.76 (d, J = 3.0 Hz, 1H, H-3$_B$), 4.71 (d, J = 11.2 Hz, 1H, C*H*HPh), 4.63−4.57 (m, 2H, H-5$_A$, H-4$_B$), 4.48−4.38 (m, 4H, C*H*$_2$Ph, H-1aAll, H-6a$_B$), 4.34−4.25 (m, 2H, H-6b$_B$, H-1bAll), 4.10 (dd, J = 9.3, 2.8 Hz, 1H, H-3$_A$), 4.02 (t, J = 9.3 Hz, 1H, H-4$_A$), 3.67−3.58 (m, 2H, H-7ab$_A$), 2.52−2.45 (m, 1H, H-6a$_A$), 2.02−1.93 (m, 1H, H-6b$_A$), 1.57 (s, 3H, C*H*$_3$), 1.55 (s, 3H, C*H*$_3$), 1.43 (s, 3H, C*H*$_3$), 1.11 (s, 3H, C*H*$_3$); ^{13}C NMR (100 MHz, py-d_5) δ 139.8−133.9 (6 × C-Ar), 135.8 (C-2All), 132.3−124.2 (*C*H-Ar), 117.3 (C-3All), 112.2 (C-iso), 109.8 (C-iso), 106.3 (C-1$_B$), 105.3 (*C*H-acetal), 87.9 (C-1$_A$), 84.1 (C-2$_B$), 82.1 (C-4$_B$), 80.6 (C-3$_A$), 79.6 (C-4$_A$), 79.5 (C-3$_B$), 76.3 (C-2$_A$), 75.6 (*C*H$_2$Ph), 73.9 (C-5$_B$), 73.3 (*C*H$_2$Ph), 71.5 (C-1All), 70.6 (C-5$_A$), 67.9 (C-6$_B$), 67.3 (C-7$_A$), 32.7 (C-6$_A$), 27.4−26.1 (4 × CH_3); MS (ESI-TOF) m/z = 927.8 [M + Na]$^+$; HRMS (ESI-TOF) m/z [M + NH_4]$^+$ calcd for $C_{53}H_{64}NO_{11}S$, 922.4195; found, 922.4190.

2-Naphthaldehyde(1-adamantanyl)(phenyl 3-*O*-allyl-4,7-di-*O*-benzyl-6-deoxy-1-thio-α-D-*manno*-heptopyranosid-2-yl) Acetal (38). According to the general procedure for the synthesis of mixed acetals, donor **25** (15 mg, 23 μmol) was reacted with acceptor **44** (5.3 mg, 35 μmol, 1.5 equiv) in the presence of DDQ (6.3 mg, 28 μmol, 1.2 equiv). Purification by silica gel flash chromatography (PE/EtOAc 10:0 to 8:2 + 5% Et_3N) gave **38** (7.2 mg, 40%) as a white solid: R_f 0.6 (PE/EtOAc 8:2); $[\alpha]_D^{20}$ = +159.7 (c 0.1, $CHCl_3$); HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{51}H_{57}O_6S$, 797.3870; found, 797.3851. The mixed acetals were unstable and decomposed in the NMR tube ($CDCl_3$ or py-d_5).

2-Naphthaldehyde(stigmastan-3-yl)(phenyl 3-*O*-allyl-4,7-di-*O*-benzyl-6-deoxy-1-thio-α-D-*manno*-heptopyranosid-2-yl) Acetal (39). According to the general procedure for the synthesis of

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mixed acetals, donor **25** (20.2 mg, 31 μmol) was reacted with acceptor **43** (14 mg, 34 μmol, 1.1 equiv) in the presence of DDQ (8.4 mg, 37 μmol, 1.2 equiv). Purification by silica gel flash chromatography (PE/EtOAc 10:0 to 95:5 + 5% Et_3N) gave **39** (15 mg, 44%) as a yellow oil: R_f 0.6 (PE/EtOAc 8:2); $[\alpha]_D^{20}$ = +55.0 (*c* 0.3, $CHCl_3$); HRMS (ESI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{70}H_{93}O_6S$ 1061.6687, found 1061.6677. The mixed acetals were unstable and decomposed in the NMR tube ($CDCl_3$ and py-d_5).

(5-Amino-*N*-benzyloxycarbonyl-1-pentyl) 4,7-Di-*O*-benzyl-3-*O*-*tert*-butyldimethylsilyl-6-deoxy-β-D-*manno*-heptopyranoside (45). To a solution of acetal **33** (88 mg, 92 μmol, 1.0 equiv) in anhydrous DCE (9.2 mL) were added DTBMP (76 mg, 0.37 mmol, 4.0 equiv) and freshly activated 4 Å powdered molecular sieves (250 mg). The suspension was stirred for 40 min at rt under Ar. Then, MeOTf (35 μL, 0.31 mmol, 3.4 equiv) was added, and the mixture was stirred for 48 h at 40 °C under Ar. After the mixture was cooled to rt, the reaction was quenched with Et_3N (2 mL), stirred for another 10 min, diluted with EtOAc (10 mL), and filtered over Celite. The filtrate was concentrated under reduced pressure and purified by silica gel flash chromatography (pentane/EtOAc 95:5 to 80:20) to give **45** (16.3 mg, 25%) as a colorless oil: R_f 0.2 (PE/EtOAc 7:3); $[\alpha]_D^{20}$ = −11.3 (*c* 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27−7.11 (m, 15H, C*H*-Ar), 4.98 (s, 2H, CO_2CHHPh), 4.72 (d, *J* = 11.3 Hz, 1H, CH_2Ph), 4.45 (d, *J* = 11.1 Hz, 1H, C*H*HPh), 4.41 (d, *J* = 12 Hz, 1H, C*H*HPh), 4.30 (d, *J* = 12.0 Hz, 1H, C*H*HPh), 4.28 (s, 1H, H-1), 3.76 (s, 1H, H-2), 3.69−3.62 (m, 2H, H-1a$_{linker}$, H-3), 3.55−3.43 (m, 2H, H-7ab), 3.36−3.22 (m, 3H, H-4, H-5, H-1b$_{linker}$), 3.07 (d, *J* = 6.1 Hz, 1H, H-5$_{linker}$), 2.12−2.05 (m, 1H, H-6a), 1.64−1.56 (m, 1H, H-6b), 1.54−1.46 (m, 2H, H-2$_{linker}$), 1.42−1.35 (m, 2H, H-4$_{linker}$), 1.29−1.23 (m, 2H, H-3$_{linker}$), 0.83 (s, 9H, C(CH_3)$_3$), 0.01 (s, 3H, CH_3Si), 0.00 (s, 3H, CH_3Si); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.5 (CO), 138.7−136.7 (3 × C-Ar), 128.6−127.6 (CH-Ar), 99.9 (C-1), 79.4 (C-4), 75.8 (C-3), 75.4 (CH_2Ph), 72.9 (CH_2Ph), 72.0 (C-2), 71.8 (C-5), 69.7 (C-1$_{linker}$), 66.7 (CO_2CH_2Ph), 66.4 (C-7), 41.0 (C-5$_{linker}$), 31.8 (C-6), 29.8 (C-4$_{linker}$), 29.3 (C-2$_{linker}$), 25.9 (C(CH_3)$_3$), 18.1 (C(CH_3)$_3$), −4.4 (CH_3Si), −4.5 (CH_3Si); MS (ESI-TOF) *m*/*z* 730.9 $[M + Na]^+$; HRMS (ESI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{40}H_{58}NO_8Si$, 708.3926; found, 708.3924.

General Procedure for IAD from Isolated Mixed Acetals 34−39. To a solution of mixed acetals (1.0 equiv) and DTBMP (3.0 equiv) in anhydrous DCE (100 mL·mmol^{-1}) was added freshly activated 5 Å powdered molecular sieves (4 mg·mg^{-1} of acetal). The suspension was stirred for 50 min at rt under Ar. Me_2S_2 (3.0 equiv) followed by MeOTf (3.0 equiv) was then injected, keeping rigorous anhydrous conditions. The mixture was stirred for 24 h at 40 °C under Ar. After the mixture was cooled to rt, the reaction was quenched with Et_3N, stirred for 10 min, diluted with DCM, and filtered over Celite. The filtrate was concentrated under reduced pressure and purified by silica gel flash chromatography.

(5-Amino-*N*-benzyloxycarbonyl-1-pentyl) 3-*O*-Allyl-4,7-di-*O*-benzyl-6-deoxy-β-D-*manno*-heptopyranoside (46). The title compound was synthesized from acetals **34** (15.8 mg, 18 μmol) according to the general procedure for IAD from isolated mixed acetals. Purification by silica gel flash chromatography (PE/EtOAc 95:5 to 60:40) gave **46** (5.1 mg, 45%) as a colorless oil: R_f 0.2 (PE/EtOAc 6:4); $[\alpha]_D^{20}$ = −10.2 (*c* 0.2, $CHCl_3$); ^{1}H NMR (400 MHz, py-d_5) δ 7.54−7.28 (m, 15H, C*H*-Ar), 6.13−6.04 (m, 1H, H-2all), 5.45 (ddd, *J* = 17.2, 4.0, 1.8 Hz, 1H, H-3aAll), 5.36 (s, 2H, CO_2CH_2Ph), 5.20 (d, *J* = 11.3 Hz, 1H, C*H*HPh), 5.17 (ddd, *J* = 10.5, 3.6, 1.2 Hz, 1H, H-3bAll), 4.79 (d, *J* = 11.3 Hz, 1H, C*H*HPh), 4.60 (d, *J* = 12.1 Hz, 1H, C*H*HPh), 4.56 (s, 1H, H-1), 4.51 (d, *J* = 12.1 Hz, 1H, CH*H*Ph), 4.47 (d, *J* = 2.8 Hz, 1H, H-2), 4.43 (ddt, *J* = 13.0, 5.2, 1.9 Hz, 1H, H-1aAll), 4.22 (ddt, *J* = 13.0, 5.3, 1.9 Hz, 1H, H-1bAll), 4.06 (t, *J* = 9.3 Hz, 1H, H-4), 3.96 (dt, *J* = 9.6, 6.4 Hz, 1H, H-1a$_{linker}$), 3.88 (td, *J* = 8.9, 5.9 Hz, 1H, H-7a), 3.78−3.74 (m, 2H, H-7b, H-3), 3.73 (dd, *J* = 9.6, 2.5 Hz, 1H, H-5), 3.53 (dt, *J* = 9.5, 6.4 Hz, 1H, H-1b$_{linker}$), 3.36 (dd, *J* = 13.0, 6.7 Hz, 2H, H-5$_{linker}$), 2.55−2.48 (m, 1H, H-6a), 2.00−1.91 (m, 1H, H-6b), 1.67−1.58 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.49−1.43 (m, 2H, H-3$_{linker}$); ^{13}C NMR (100 MHz, py-d_5) δ 157.1 (CO_2CH_2Ph), 139.7−138.2 (3 × C-Ar), 135.9 (C-2All), 128.7−123.7 (CH-Ar), 116.2 (C-3All), 101.4 (C-1, $^1J_{C1,H1}$ = 155 Hz), 83.3 (C-3), 78.8 (C-4), 75.1 (CH_2Ph), 72.8 (CH_2Ph), 72.4 (C-5), 69.8 (C-1All), 69.3 (C-1$_{linker}$), 68.4 (C-2), 66.9 (C-7), 66.1 (CO_2CH_2Ph), 41.2 (C-5$_{linker}$), 32.7 (C-6), 30.2 (C-2$_{linker}$), 29.8 (C-4$_{linker}$), 23.8 (C-3$_{linker}$); MS (ESI-TOF) *m*/*z* = 656.7 $[M + Na]^+$; HRMS (ESI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{37}H_{48}NO_8$, 634.3374; found, 634.3369.

(5-Azido-1-pentyl) 3-*O*-Allyl-4,7-di-*O*-benzyl-6-deoxy-β-D-*manno*-heptopyranoside (47). The title compound was synthesized from acetals **35** (340 mg, 430 μmol) according to the general procedure for IAD from isolated mixed acetals. Purification by silica gel flash chromatography (PE/EtOAc 9:1 to 7:3) gave **47** (142 mg, 62%) as a colorless oil: R_f 0.2 (PE/EtOAc 8:2); $[\alpha]_D^{20}$ = −29.6 (*c* 0.02, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.23 (m, 10H, C*H*-Ar), 6.00−5.90 (m, 1H, H-2All), 5.31 (ddd, *J* = 17.1, 3.6, 1.5 Hz, 1H, H-3aAll), 5.20 (ddd, *J* = 10.4, 3.3, 1.2 Hz, 1H, H-3bAll), 4.90 (d, *J* = 10.8 Hz, 1H, C*H*HPh), 4.61 (d, *J* = 10.8 Hz, 1H, C*H*HPh), 4.53 (d, *J* = 12.1 Hz, 1H, C*H*HPh), 4.43 (d, *J* = 12.1 Hz, 1H, C*H*HPh), 4.35 (s, 1H, H-1), 4.23 (ddt, *J* = 12.7, 5.8, 1.2 Hz, 1H, H-1aAll), 4.13 (ddt, *J* = 12.5, 5.6, 1.1 Hz, 1H, H-1bAll), 4.08 (d, *J* = 2.3 Hz, 1H, H-2), 3.79 (dt, *J* = 9.4, 6.4 Hz, 1H, H-1a$_{linker}$), 3.68−3.57 (m, 2H, H-7ab), 3.53 (t, *J* = 9.1 Hz, 1H, H-4), 3.47 (dd, *J* = 8.8, 2.9 Hz, 1H, H-3), 3.44−3.35 (m, 2H, H-1b$_{linker}$, H-5), 3.26 (t, *J* = 6.7 Hz, 2H, H-5$_{linker}$), 2.30−2.23 (m, 1H, H-6a), 1.79−1.71 (m, 1H, H-6b), 1.65−1.56 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.46−1.39 (m, 2H, H-3$_{linker}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6−138.3 (2 × C-Ar), 134.6 (C-2All), 128.4−127.5 (CH-Ar), 117.6 (C-3All), 99.7 (C-1, $^1J_{C,H}$ = 156 Hz), 81.7 (C-3), 77.9 (C-4), 75.3 (CH_2Ph), 72.8 (CH_2Ph), 71.8 (C-5), 70.7 (C-1All), 69.3 (C-1$_{linker}$), 68.5 (C-2), 66.2 (C-7), 51.3 (C-5$_{linker}$), 31.8 (C-6), 29.1 (C-2$_{linker}$), 28.6 (C-4$_{linker}$), 23.3 (C-3$_{linker}$); MS (ESI-TOF) *m*/*z* = 543.7 $[M + NH_4]^+$, *m*/*z* = 548.6 $[M + Na]^+$; HRMS (ESI-TOF) *m*/*z* $[M + NH_4]^+$ calcd for $C_{29}H_{43}N_4O_6$, 543.3177; found, 543.3177.

3-*O*-Allyl-4,7-di-*O*-benzyl-6-deoxy-β-D-*manno*-heptopyranosyl-[1→6]-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (50). The title compound was synthesized from acetals **36** (17.4 mg, 19 μmol) according to the general procedure for IAD from isolated mixed acetals. Purification by silica gel flash chromatography (PE/EtOAc 9:1 to 5:5) gave **50** (7.7 mg, 62%) as a yellow oil. R_f 0.1 (PE/EtOAc 6:4); $[\alpha]_D^{20}$ = −34.4 (*c* 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.26 (m, 10H, C*H*-Ar), 5.99−5.89 (m, 1H, H-2All), 5.53 (d, *J* = 5.0 Hz, 1H, H-1$_B$), 5.30 (ddd, *J* = 17.1, 4.7, 1.6 Hz, 1H, H-3aAll), 5.19 (ddd, *J* = 10.4, 3.9, 1.5 Hz, 1H, H-3bAll), 4.91 (d, *J* = 10.9 Hz, 1H, C*H*HPh), 4.61 (d, *J* = 10.9 Hz, 1H, C*H*HPh), 4.58 (dd, *J* = 8.3, 2.5 Hz, 1H, H-3$_B$), 4.51 (d, *J* = 11.9 Hz, 1H, C*H*HPh), 4.49 (d, *J* = 0.7 Hz, 1H, H-1$_A$), 4.46 (d, *J* = 11.9 Hz, 1H, C*H*HPh), 4.30 (dd, *J* = 5.1, 2.4 Hz, 1H, H-2$_B$), 4.22 (ddt, *J* = 12.6, 5.7, 1.3 Hz, 1H, H-1aAll), 4.17 (dd, *J* = 7.8, 1.5 Hz, 1H, H-4$_B$), 4.16 (br s, 1H, H-2$_A$), 4.10 (ddt, *J* = 12.6, 5.7, 1.3 Hz, 1H, H-1bAll), 4.04−3.98 (m, 2H, H-6a$_B$, H-5$_B$), 3.68 (dd, *J* = 11.8, 3.2 Hz, 1H, H-6b$_B$), 3.65−3.60 (m, 2H, H-7ab$_A$), 3.56 (t, *J* = 9.2 Hz, 1H, H-4$_A$), 3.46 (dd, *J* = 9.1, 3.1 Hz, 1H, H-3$_A$), 3.38 (td, *J* = 9.5, 2.6 Hz, 1H, H-5$_A$), 2.29−2.22 (m, 1H, H-6a$_A$), 1.83−1.74 (m, 1H, H-6b$_A$), 1.52 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.32 (s, 3H, CH_3), 1.25 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5−138.4 (2 × C-Ar), 134.6 (C-2All), 128.3−127.5 (CH-Ar), 117.5 (C-3All), 109.4 (C-iso), 108.7 (C-iso), 100.1 (C-1$_A$, $^1J_{C,H}$ = 158 Hz), 96.3 (C-1$_B$), 81.5 (C-3$_A$), 77.9 (C-4$_A$), 75.3 (CH_2Ph), 72.8 (CH_2Ph), 72.1 (C-5$_A$), 71.4 (C-4$_B$), 70.7 (C-3$_B$), 70.6 (C-1All), 70.4 (C-2$_B$), 68.8 (C-6$_B$), 68.3 (C-2$_A$), 67.8 (C-5$_B$), 66.5 (C-7$_A$), 31.9 (C-6$_A$), 26.1−24.4 (4 × CH_3); HRMS (ESI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{36}H_{49}O_{11}$, 657.3269; found, 657.3267.

3-*O*-Allyl-4,7-di-*O*-benzyl-6-deoxy-β-D-*manno*-heptopyranosyl-[1→3]-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (51). The title compound was synthesized from acetals **37** (10 mg, 11 μmol) according to the general procedure for IAD from isolated mixed acetals. Purification by silica gel flash chromatography (PE/EtOAc 9:1 to 6:4) gave **51** (3.3 mg, 46%) as a yellow oil: R_f 0.2 (PE/EtOAc 6:4); $[\alpha]_D^{20}$ = −3.1 (*c* 0.06, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.25 (m, 10H, C*H*-Ar), 6.00−5.90 (m, 1H, H-2All), 5.88 (d, *J* = 3.7 Hz, 1H, H-1$_B$), 5.31 (ddd, *J* = 17.1, 3.9, 1.5 Hz, 1H, H-3aAll), 5.20 (ddd, *J* = 10.4, 3.3, 1.2 Hz, 1H, H-3bAll), 4.91 (d, *J* = 10.9 Hz, 1H, C*H*HPh), 4.61 (d, *J* = 10.9 Hz, 1H, C*H*HPh), 4.59 (s, 1H, H-1$_A$), 4.53

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(d, J = 11.9 Hz, 1H, C*H*HPh), 4.48 (s, 1H, H-3_B), 4.47 (s, 1H, H-2_B), 4.46 (d, J = 11.9 Hz, 1H, C*H*HPh), 4.34 (dd, J = 12.3, 6.2 Hz, 1H, H-5_B), 4.25−4.20 (m, 2H, H-4_B, H-1aAll), 4.16−4.10 (m, 2H, H-$6a_B$, H-1bAll), 4.05−3.99 (m, 2H, H-2_A, H-$6b_B$), 3.67−3.60 (m, 2H, H-$7ab_A$), 3.57 (t, J = 9.3 Hz, 1H, H-4_A), 3.48 (dd, J = 8.7, 2.9 Hz, 1H, H-3_A), 3.40 (dd, J = 9.5, 2.5 Hz, 1H, H-5_A), 2.30−2.22 (m, 1H, H-$6a_A$), 1.84−1.76 (m, 1H, H-$6b_A$), 1.50 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.27 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5−138.3 (2 × C-Ar), 134.6 (C-2All), 128.4−127.6 (*C*H-Ar), 117.6 (C-3All), 111.9 (C-iso), 109.0 (C-iso), 105.2 (C-1_B), 97.6 (C-1_A, $^1J_{C,H}$ = 156 Hz), 83.2 (C-2_B), 81.4 (C-3_A), 80.5 (C-4_B), 78.5 (C-3_B), 77.6 (C-4_A), 75.3 (*C*H_2Ph), 73.3 (C-5_B), 72.9 (*C*H_2Ph), 72.5 (C-5_A), 70.8 (C-1All), 68.9 (C-2_B), 66.7 (C-6_B), 66.2 (C-7_A), 31.8 (C-6_A), 26.8−25.4 (4 × CH_3); HRMS (ESI-TOF) m/z [M + NH_4]$^+$ calcd for $C_{36}H_{52}NO_{11}$, 674.3535; found, 674.3533.

(1-Adamantanyl) 3-*O*-Allyl-4,7-di-*O*-benzyl-6-deoxy-β-D-*manno*-heptopyranoside (52). *Representative Procedure for the One-Pot IAD.* To a mixture of donor **25** (25 mg, 40 μmol, 1.0 equiv) and acceptor **44** (8.8 mg, 0.06 mmol, 1.5 equiv) in anhydrous DCM (800 μL) was added freshly activated 4 Å powdered molecular sieves (100 mg). The mixture was stirred at rt for 40 min under Ar. Then, DDQ (11 mg, 50 μmol, 1.3 equiv) was added, and the deep-green mixture was stirred for 1 h at rt under Ar. The reaction was quenched by adding a saturated $NaHCO_3$(aq) solution (3 mL) and stirred until the color turned to bright yellow (∼10 min). The solution was diluted with DCM (10 mL) and filtered over Celite. The organic phase was washed with a saturated $NaHCO_3$(aq) solution (5 mL) and brine (5 mL). The solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure and coevaporated with toluene (3×). To a solution of crude acetals **38** in anhydrous DCE (9.7 mL) were added DTBMP (24 mg, 120 μmol, 3.0 equiv) and freshly activated 5 Å powdered molecular sieves (124 mg). The suspension was stirred for 50 min at rt under Ar. Me_2S_2 (10.5 μL, 0.12 mmol, 3.0 equiv) and MeOTf (13.2 μL, 0.12 mmol, 3.0 equiv) were then injected to the mixture, which was stirred for 20 h at 40 °C. After cooling to rt, the reaction was quenched by adding Et_3N, stirred for 10 min, diluted with DCM (10 mL), and filtered over Celite. The filtrate was concentrated under reduced pressure and purified by silica gel flash chromatography (PE/EtOAc 10:0 to 6:4) to give **52** (12.1 mg, 58%, two steps) as a colorless oil: R_f 0.1 (PE/EtOAc 6:4); $[\alpha]_D^{20}$ = −14.8 (c = 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.24 (m, 10H, C*H*-Ar), 6.00−5.91 (m, 1H, H-2All), 5.31 (ddd, J = 17.2, 3.6, 1.6 Hz, 1H, H-3aAll), 5.20 (ddd, J = 10.4, 3.2, 1.5 Hz, 1H, H-3bAll), 4.90 (d, J = 10.9 Hz, 1H, C*H*HPh), 4.68 (d, J = 0.9 Hz, 1H, H-1), 4.61 (d, J = 10.9 Hz, 1H, C*H*HPh), 4.46 (s, 2H, CH_2Ph), 4.24 (ddt, J = 12.7, 5.8, 1.4 Hz, 1H, H-1aAll), 4.13 (ddt, J = 12.7, 5.7, 1.4 Hz, 1H, H-1bAll), 3.94 (dd, J = 3.1, 0.9 Hz, 1H, H-2), 3.63−3.59 (m, 2H, H-7ab), 3.52 (t, J = 9.1 Hz, 1H, H-4), 3.48 (dd, J = 8.9, 3.0 Hz, 1H, H-3), 3.38 (td, J = 9.8, 2.4 Hz, 1H, H-5), 2.27−2.16 (m, 1H, H-6a), 2.11 (s, 3H, 3 × C*H*-ada), 1.84−1.73 (m, 6H, 3 × CH_2-ada), 1.70−1.66 (m, 1H, H-6b), 1.63−1.54 (m, 6H, 3 × CH_2-ada); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6−138.5 (2 × C-Ar), 134.8 (C-2All), 128.4−127.6 (*C*H-Ar), 117.6 (C-3All), 92.8 (C-1, $^1J_{C,H}$ = 155 Hz), 82.1 (C-3), 78.1 (C-4), 75.4 (*C*H_2Ph), 75.3 (C-Ada), 72.9 (*C*H_2Ph), 71.5 (C-5), 70.7 (C-1All), 70.2 (C-2), 66.7 (C-7), 42.5 (3 × *C*H_2-ada), 36.3 (3 × *C*H_2-ada), 31.7 (C-6), 30.7 (3 × *C*H-ada); HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{34}H_{48}NO_6$, 566.3476; found, 566.3472.

(Stigmastan-3-yl) 3-*O*-Allyl-4,7-di-*O*-benzyl-6-deoxy-β-D-*manno*-heptopyranoside (53). The title compound was synthesized from acetals **39** (14.6 mg, 0.014 mmol) according to the general procedure for IAD from isolated mixed acetals. Purification by silica gel flash chromatography (PE/EtOAc 9:1 to 7:3) gave **53** (8.5 mg, 75%) as a colorless oil: R_f 0.2 (PE/EtOAc 7:3); $[\alpha]_D^{20}$ = +12.8 (c 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.28 (m, 10H, C*H*-Ar), 6.00−5.91 (m, 1H, H-2all), 5.31 (ddd, J = 17.3, 3.6, 1.6 Hz, 1H, H-3aAll), 5.20 (ddd, J = 10.4, 3.1, 1.6 Hz, 1H, H-3bAll), 4.90 (d, J = 10.9 Hz, 1H, C*H*HPh), 4.61 (d, J = 10.9 Hz, 1H, C*H*HPh), 4.51 (s, 1H, H-1), 4.50 (d, J = 11.9 Hz, 1H, C*H*HPh), 4.45 (d, J = 11.9 Hz, 1H, C*H*HPh), 4.23 (ddt, J = 12.8, 5.8, 1.3 Hz, 1H, H-1aAll), 4.12 (ddt, J = 12.7, 5.8, 1.3 Hz, 1H, H-1bAll), 4.03 (d, J = 3.0 Hz, 1H, H-2), 3.64−3.58 (m, 2H, H-7ab), 3.54 (t, J = 9.2 Hz, 1H, H-4), 3.46 (dd, J = 8.9, 3.1 Hz, 1H, H-3), 3.37 (td, J = 9.6, 2.5 Hz, 1H, H-5), 2.30−2.23 (m, 1H, H-6a), 1.96−1.79 (m, 4H, 2 × CH_2-stig), 1.78−1.72 (m, 1H, H-6b), 1.71−1.41 (m, 11H, C*H*-stig, 5 × CH_2-stig), 1.35−0.94 (m, 19H, 5 × C*H*-stig, 7 × CH_2-stig), 0.94−0.92 (m, 1H, C*H*-stig), 0.90 (d, J = 6.5 Hz, 3H, CH_3-stig), 0.85 (d, J = 7.5 Hz, 3H, CH_3-stig), 0.82 (s, 3H, CH_3-stig), 0.81 (d, J = 6.9 Hz, 3H, CH_3-stig), 0.77 (s, 3H, CH_3-stig), 0.64 (s, 3H, CH_3-stig), 0.63−0.56 (m, 1H, C*H*-stig); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7, 138.5 (2 × C-Ar), 134.8 (C-2All), 128.5−127.6 (*C*H-Ar), 117.6 (C-3All), 97.4 (C-1, $^1J_{C,H}$ = 157 Hz), 81.8 (C-3), 77.9 (C-4), 75.3 (*C*H_2Ph), 72.8 (*C*H_2Ph), 71.7 (C-5), 70.6 (C-1All), 69.1 (C-2), 66.5 (C-7), 56.5, 56.1, 54.3, 45.8, 44.7 (5 × *C*H-stig), 42.7 (C-stig), 40.0, 36.9 (2 × *C*H_2-stig), 36.1 (*C*H-stig), 35.6 (C-stig), 35.4 (*C*H-stig), 34.3, 33.9, 32.1 (3 × *C*H_2-stig), 31.7 (C-6), 29.7, 29.2 (2 × *C*H_2-stig), 29.1 (*C*H-stig), 28.8, 26.0, 24.2, 23.0, 21.2 (5 × *C*H_2-stig), 19.8, 19.0, 18.7, 12.2, 12.1, 11.9 (6 × *C*H_3-stig); HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{53}H_{81}O_6$, 813.6028; found, 813.6011.

(5-Azido-1-pentyl) 3-*O*-Allyl-4,7-di-*O*-benzyl-6-deoxy-α-D-*manno*-heptopyranosyl-[1→2]-3-*O*-allyl-4,7-di-*O*-benzyl-6-deoxy-β-D-*manno*-heptopyranoside (49). The title compound was isolated as a byproduct along with β-glycoside **47** from the reaction of mixed acetal **35** (280 mg, 360 μmol) according to the general procedure for IAD from isolated mixed acetals. Freshly activated 4 Å powdered molecular sieves was used instead of 5 Å MS. Purification by silica gel flash chromatography (PE/EtOAc 9:1 to 6:4) gave **47** (66 mg, 35%) as a major compound along with **49** (11 mg, 3%), both as colorless oils. Analytical data for **49**: R_f 0.1 (PE/EtOAc 7:3); $[\alpha]_D^{20}$ = −19.6 (c 0.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.22 (m, 20H, C*H*-Ar), 5.96−5.88 (m, 2H, 2 × H-2All), 5.28 (ddd, J = 17.3, 3.7, 1.6 Hz, 2H, 2 × H-3aAll), 5.16 (ddd, J = 10.4, 3.4, 1.2 Hz, 2H, 2 × H-3bAll), 4.95 (d, J = 10.9 Hz, 1H, C*H*HPh), 4.89 (d, J = 10.9 Hz, 1H, C*H*HPh), 4.82 (s, 1H, H-1_B), 4.61 (d, J = 11.1 Hz, 1H, C*H*HPh), 4.58 (d, J = 10.9 Hz, 1H, C*H*HPh), 4.53 (d, J = 12.1 Hz, 1H, C*H*HPh), 4.51 (d, J = 12.0 Hz, 1H, C*H*HPh), 4.44 (d, J = 12.0 Hz, 1H, C*H*HPh), 4.41 (d, J = 12.0 Hz, 1H, C*H*HPh), 4.27 (ddt, J = 12.8, 5.6, 1.4 Hz, 1H, H-1aAll), 4.26 (s, 1H, H-1_A), 4.22 (d, J = 3.2 Hz, 1H, H-2_B), 4.20 (d, J = 2.6 Hz, 1H, H-2_A), 4.18 (ddt, J = 12.0, 5.3, 1.4 Hz, 1H, H-1aAll), 4.09 (ddt, J = 12.8, 5.8, 1.3 Hz, 1H, H-1bAll), 3.88 (ddt, J = 12.3, 5.9, 1.3 Hz, 1H, H-1bAll), 3.74 (td, J = 9.3, 6.4 Hz, 1H, H-$1a_{linker}$), 3.67−3.55 (m, 5H, H-4_A, H-$7ab_A$, H-$7ab_B$), 3.47−3.30 (m, 6H, H-4_B, H-3_A, H-3_B, H-5_A, H-5_B, H-$1b_{linker}$), 3.20 (t, J = 6.8 Hz, 2H, H-5_{linker}), 2.31−2.22 (m, 2H, H-$6a_A$, H-$6a_B$), 1.85−1.68 (m, 2H, H-$6b_A$, H-$6b_B$), 1.59−1.51 (m, 4H, H-2_{linker}, H-4_{linker}), 1.40−1.34 (m, 2H, H-3_{linker}); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6−138.4 (4 × C-Ar), 134.8−134.6 (2 × C-2All), 128.3−127.5 (*C*H-Ar), 117.3−117.2 (2 × C-3All), 100.1 (C-1_A, $^1J_{C,H}$ = 155 Hz), 98.9 (C-1_B, $^1J_{C,H}$ = 164 Hz), 81.6 (C-3_A), 80.5 (C-3_B), 77.7 (C-4_A, C-4_B), 75.4 (*C*H_2Ph), 75.3 (*C*H_2Ph), 72.8 (*C*H_2Ph), 72.7 (*C*H_2Ph), 72.4 (C-5_B), 72.1 (C-5_A), 70.4 (C-2_B), 70.3 (C-1All), 69.6 (C-1All), 69.4 (C-1_{linker}), 68.0 (C-2_A), 66.7 (C-7_A*), 66.3 (C-7_B*), 51.2 (C-5_{linker}), 31.9 (C-6_A), 31.8 (C-6_B), 29.2 (C-2_{linker}), 28.5 (C-4_{linker}), 23.3 (C-3_{linker}); MS (ESI-TOF) m/z = 945.2 [M + Na]$^+$; HRMS (ESI-TOF) m/z [M + NH_4]$^+$ calcd for $C_{53}H_{71}N_4O_{11}$, 939.5114; found, 939.5111.

(5-Azido-1-pentyl) 2-*O*-Acetyl-3-*O*-allyl-4,7-di-*O*-benzyl-6-deoxy-β-D-*manno*-heptopyranoside (54). To a solution of alcohol **47** (483 mg, 0.92 mmol, 1.0 equiv) in anhydrous py (15.4 mL) were added Ac_2O (15.4 mL) and cat. DMAP (11 mg, 92 μmol, 0.1 equiv). The mixture was stirred at rt for 15 min under N_2. Then, the mixture was concentrated under reduced pressure and coevaporated with toluene (3×). The residue was purified by silica gel flash chromatography (PE/EtOAc 95:5 to 80:20) to give **54** (475 mg, 91%) as a yellow oil: R_f 0.4 (PE/EtOAc 8:2); $[\alpha]_D^{20}$ = −20.1 (c 0.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.27 (m, 10H, C*H*-Ar), 5.93−5.84 (m, 1H, H-2All), 5.48 (dd, J = 3.4, 1.0 Hz, 1H, H-2), 5.29 (ddd, J = 17.2, 3.7, 1.6 Hz, 1H, H-3aAll), 5.17 (ddd, J = 10.3, 3.2, 1.2 Hz, 1H, H-3bAll), 4.90 (d, J = 10.7 Hz, 1H, C*H*HPh), 4.60 (d, J = 10.7 Hz, 1H, C*H*HPh), 4.53 (d, J = 12.0 Hz, 1H, C*H*HPh), 4.43 (d, J = 12.0 Hz, 1H, C*H*HPh), 4.42 (d, J = 1.0 Hz, 1H, H-1), 4.18 (ddt, J = 12.5, 5.4, 1.4 Hz, 1H, H-1aAll), 4.00 (ddt, J = 12.5, 5.9, 1.3 Hz, 1H, H-1bAll), 3.74 (td, J = 9.3, 6.3 Hz, 1H, H-$1a_{linker}$), 3.64−3.55 (m, 2H, H-

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7ab), 3.55−3.52 (m, 1H, H-3), 3.46−3.41 (m, 2H, H-4, H-5), 3.38 (td, J = 9.4, 6.6 Hz, 1H, H-1b$_{linker}$), 3.24 (t, J = 6.9 Hz, 1H, H-5$_{linker}$), 2.34−2.26 (m, 1H, H-6a), 2.18 (s, 3H, CH_3CO), 1.81−1.73 (m, 1H, H-6b), 1.62−1.53 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.42−1.33 (m, 2H, H-3$_{linker}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7 (CO), 138.7−138.4 (2 × C-Ar), 134.5 (C-2All), 128.5−127.7 (CH-Ar), 117.6 (C-3All), 99.0 (C-1), 80.3 (C-3), 78.2 (C-4), 75.4 (CH_2Ph), 72.9 (CH_2Ph), 72.2 (C-5), 70.6 (C-1All), 69.6 (C-1$_{linker}$), 68.5 (C-2), 66.3 (C-7), 51.4 (C-5$_{linker}$), 31.9 (C-6), 29.1 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 23.3 (C-3$_{linker}$), 21.2 (CH$_3$CO); HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{31}H_{42}N_3O_7$, 568.3017; found, 568.3013.

(5-Azido-1-pentyl) 2-*O*-Acetyl-4,7-di-*O*-benzyl-6-deoxy-β-D-*manno*-heptopyranoside (55). To a solution of **54** (10 mg, 18 μmol, 1.0 equiv) in anhydrous MeOH (900 μL) was added $PdCl_2$ (2 mg, 13 μmol, 0.6 equiv). The mixture was stirred for 4 h at 40 °C under N_2. Then, the mixture was cooled to rt, diluted with DCM (5 mL), and filtered over Celite. The filtrate was concentrated under reduced pressure and coevaporated with toluene (3×). Crude alcohol **55** was used for the next step without further purification to avoid acetyl migration between the C2 and C3 positions. For analytical measurements, the residue was purified by silica gel flash chromatography (PE/EtOAc 10:0 to 6:4) to give **55** (5.1 mg, 55%) as a yellow oil in a mixture of C2/C3 regioisomers (ratio C2/C3 ∼ 2.8:1.0): R_f 0.1 (PE/EtOAc 7:3); $[\alpha]_D^{20}$ = −16.9 (c 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.27 (m, 10H, CH-Ar), 5.35 (dd, J = 3.5, 0.9 Hz, 1H, H-2), 4.80 (d, J = 11.1 Hz, 1H, CHHPh), 4.70 (d, J = 11.1 Hz, 1H, CHHPh), 4.55 (d, J = 12.0 Hz, 1H, CHHPh), 4.47 (d, J = 1.0 Hz, 1H, H-1), 4.44 (d, J = 12.0 Hz, 1H, CHHPh), 3.85 (br d, J = 8.4 Hz, 1H, H-3), 3.78−3.72 (m, 1H, H-1a$_{linker}$), 3.70−3.62 (m, 2H, H-7ab), 3.45 (dd, J = 9.6, 2.2 Hz, 1H, H-5), 3.42 (t, J = 6.2 Hz, 1H, H-4), 3.39−3.36 (m, 1H, H-1b$_{linker}$), 3.25 (t, J = 6.9 Hz, 2H, H-5$_{linker}$), 2.34−2.27 (m, 1H, H-6a), 2.25 (s, 3H, CH_3CO), 1.86−1.78 (m, 1H, H-6b), 1.61−1.54 (m, 4H, H-2$_{linker}$, H-4$_{linker}$), 1.42−1.36 (m, 2H, H-3$_{linker}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3 (CO), 138.5, 138.0 (2 × C-Ar), 128.6−127.6 (CH-Ar), 98.7 (C-1), 79.7 (C-4), 75.1 (CH_2Ph), 73.3 (C-3), 72.9 (CH_2Ph), 72.0 (C-5), 71.7 (C-2), 69.5 (C-1$_{linker}$), 66.2 (C-7), 51.3 (C-5$_{linker}$), 31.9 (C-6), 28.9 (C-2$_{linker}$), 28.6 (C-4$_{linker}$), 23.3 (C-3$_{linker}$), 21.1 (CH$_3$CO); HRMS (ESI-TOF) m/z [M + NH$_4$]$^+$ calcd for $C_{28}H_{41}N_4O_7$, 545.2969; found, 545.2970.

(5-Azido-1-pentyl) 3-*O*-Allyl-4,7-di-*O*-benzyl-6-deoxy-β-D-*manno*-heptopyranosyl-[1→3]-2-*O*-acetyl-4,7-di-*O*-benzyl-6-deoxy-β-D-*manno*-heptopyranoside (56). To a mixture of donor **25** (650 mg, 1.01 mmol, 1.2 equiv) and crude acceptor **55** (442 mg, 0.838 mmol, 1.0 equiv) in anhydrous DCM (20 mL) was added freshly activated 4 Å powdered molecular sieves (2.6 g). The mixture was stirred at rt for 40 min under Ar. Then, DDQ (247 mg, 1.09 mmol, 1.3 equiv) was added, and the deep-green mixture was stirred for 3.5 h at rt under Ar. The reaction was quenched by adding a saturated $NaHCO_3$(aq) solution, stirred until the color turned bright yellow, and diluted with DCM. The mixture was filtered over Celite and rinsed with DCM, and the organic phase was washed with a saturated $NaHCO_3$(aq) solution and brine. The solvents of the dried solution ($MgSO_4$) were concentrated under reduced pressure and coevaporated with toluene (3×) to give mixed acetals as a colorless solid [R_f 0.30 (PE/EtOAc 8:2); HRMS (ESI-TOF) m/z [M + NH$_4$]$^+$ calcd for $C_{69}H_{81}N_4O_{12}S$, 1189.5566; found, 1189.5559]. Crude acetals were dissolved in anhydrous DCE (210 mL), then DTBMP (516 mg, 2.51 mmol, 3.0 equiv) and freshly activated 5 Å powdered molecular sieves (3.93 g) were added. The suspension was stirred for 50 min at rt under Ar. Me_2S_2 (226 μL, 2.51 mmol, 3.0 equiv) and MeOTf (285 μL, 2.51 mmol, 3.0 equiv) were then injected to the mixture, which was stirred for 17 h at 40 °C. After cooling to rt, the reaction was quenched by adding Et_3N, stirred for 10 min, and filtered over Celite. The filtrate was concentrated under reduced pressure and purified by silica gel flash chromatography (PE/EtOAc 9:1 to 75:25) to give disaccharide **56** (300 mg, 58%, two steps) as a colorless oil: R_f 0.2 (PE/EtOAc 7:3); $[\alpha]_D^{20}$ = −17.0 (c 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.18 (m, 20H, CH-Ar), 6.00−5.90 (m, 1H, H-2All), 5.37 (d, J = 3.5 Hz, 1H, H-2$_A$), 5.34 (ddd, J = 17.3, 3.8, 1.5 Hz, 1H, H-3aAll), 5.20 (ddd, J = 10.4, 3.3, 1.3 Hz, 1H, H-3bAll), 4.97 (d, J = 10.6 Hz, 1H, CHHPh), 4.90 (d, J = 10.9 Hz, 1H, CHHPh), 4.61 (d, J = 10.9 Hz, 1H, CHHPh), 4.58 (s, 1H, H-1$_B$), 4.57 (d, J = 10.6 Hz, 1H, CHHPh), 4.54 (d, J = 11.9 Hz, 1H, CHHPh), 4.44 (d, J = 12.1 Hz, 1H, CHHPh), 4.43 (d, J = 11.9 Hz, 1H, CHHPh), 4.36 (d, J = 12.1 Hz, 1H, CHHPh), 4.26 (s, 1H, H-1$_A$), 4.23 (ddt, J = 12.1, 5.7, 1.3 Hz, 1H, H-1aAll), 4.11 (ddt, J = 12.7, 5.6, 1.3 Hz, 1H, H-1bAll), 3.97−3.92 (m, 2H, H-3$_A$, H-2$_B$), 3.71 (td, J = 9.4, 6.3 Hz, 1H, H-1a$_{linker}$), 3.66−3.52 (m, 4H, H-7ab$_A$, H-7ab$_B$), 3.49−3.29 (m, 6H, H-3$_B$, H-4$_A$, H-4$_B$, H-5$_A$, H-5$_B$, H-1b$_{linker}$), 3.24 (t, J = 6.8 Hz, 2H, H-5$_{linker}$), 2.36−2.19 (m, 2H, H-6a$_A$, H-6a$_B$), 2.17 (s, 3H, CH_3CO), 1.83−1.77 (m, 2H, H-6b$_A$, H-6b$_B$), 1.61−1.52 (m, 4H, H-4$_{linker}$, H-2$_{linker}$), 1.40−1.32 (m, 2H, H-3$_{linker}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1 (CO), 138.7−138.5 (4 × C-Ar), 134.6 (C-2All), 128.4−127.6 (CH-Ar), 117.6 (C-3All), 98.6 (C-1$_A$, $^1J_{C,H}$ = 157 Hz), 96.7 (C-1$_B$, $^1J_{C,H}$ = 159 Hz), 81.9 (C-3$_B$), 78.0 (C-4$_A$), 77.7 (C-3$_A$), 77.1 (C-4$_B$), 75.4 (CH_2Ph), 74.7 (CH_2Ph), 72.9 (CH_2Ph), 72.7 (CH_2Ph), 72.3 (C-5$_A$), 72.1 (C-5$_B$), 70.7 (C-1All), 69.7 (C-1$_{linker}$), 68.5 (C-2$_A$), 68.4 (C-2$_B$), 66.5 (C-7$_A$), 66.3 (C-7$_B$), 51.4 (C-5$_{linker}$), 32.0 (C-6$_B$), 31.8 (C-6$_A$), 29.1 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 23.4 (C-3$_{linker}$), 21.3 (CH$_3$CO); HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{52}H_{66}N_3O_{12}$, 924.4641; found, 924.4636.

(5-Azido-1-pentyl) 2-*O*-Acetyl-3-*O*-allyl-4,7-di-*O*-benzyl-6-deoxy-β-D-*manno*-heptopyranosyl-[1→3]-2-*O*-acetyl-4,7-di-*O*-benzyl-6-deoxy-β-D-*manno*-heptopyranoside (57). To a solution of alcohol **56** (25 mg, 30 μmol, 1.0 equiv) in anhydrous py (2 mL) were added Ac_2O (2 mL) and cat. DMAP (1 mg). The mixture was stirred at rt for 30 min under N_2. The mixture was concentrated under reduced pressure and coevaporated with toluene (3×). The residue was purified by silica gel flash chromatography (PE/EtOAc 90:10 to 70:30) to give **57** (26 mg, 96%) as a yellow oil: R_f 0.2 (PE/EtOAc 7:3); $[\alpha]_D^{20}$ = −22.4 (c 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.20 (m, 20H, CH-Ar), 5.93−5.83 (m, 1H, H-2All), 5.37 (d, J = 3.0 Hz, 1H, H-2$_B$), 5.35 (d, J = 3.2 Hz, 1H, H-2$_A$), 5.31 (ddd, J = 17.3, 3.8, 1.6 Hz, 1H, H-3aAll), 5.18 (ddd, J = 10.3, 3.3, 1.4 Hz, 1H, H-3bAll), 4.93 (d, J = 10.8 Hz, 1H, CHHPh), 4.63 (s, 1H, H-1$_B$), 4.62 (d, J = 10.8 Hz, 1H, CHHPh), 4.52 (d, J = 12.1 Hz, 1H, CHHPh), 4.47 (d, J = 12.0 Hz, 1H, CHHPh), 4.45 (d, J = 10.0 Hz, 2H, CH_2Ph), 4.42 (d, J = 12.0 Hz, 1H, CHHPh), 4.37 (d, J = 12.1 Hz, 1H, CHHPh), 4.25 (s, 1H, H-1$_A$), 4.18 (ddt, J = 12.5, 5.4, 1.3 Hz, 1H, H-1aAll), 4.02 (ddt, J = 12.5, 5.8, 1.3 Hz, 1H, H-1bAll), 3.86 (dd, J = 8.5, 3.6 Hz, 1H, H-3$_A$), 3.72 (td, J = 9.4, 6.3 Hz, 1H, H-1a$_{linker}$), 3.55−3.51 (m, 5H, H-3$_B$, H-7ab$_A$, H-7ab$_B$), 3.51−3.46 (m, 2H, H-5$_B$, H-4$_B$), 3.36−3.29 (m, 3H, H-1b$_{linker}$, H-5$_A$, H-4$_A$), 3.24 (t, J = 6.8 Hz, 2H, H-5$_{linker}$), 2.33−2.24 (m, 2H, H-6a$_A$, H-6a$_B$), 2.19 (s, 3H, CH_3CO), 1.96 (s, 3H, CH_3CO), 1.82−1.71 (m, 2H, H-6b$_A$, H-6b$_B$), 1.62−1.52 (m, 4H, H-4$_{linker}$, H-2$_{linker}$), 1.42−1.33 (m, 2H, H-3$_{linker}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4 (CO), 170.1 (CO), 138.7−138.4 (4 × C-Ar), 134.3 (C-2All), 128.6−127.4 (CH-Ar), 117.4 (C-3All), 98.5 (C-1$_A$), 95.2 (C-1$_B$), 80.1 (C-3$_B$), 78.2 (C-4$_B$), 77.8 (C-3$_A$), 76.8 (C-4$_A$), 75.2 (CH_2Ph), 74.7 (CH_2Ph), 72.9 (CH_2Ph), 72.6 (CH_2Ph), 72.1 (C-5$_B$), 71.9 (C-5$_A$), 70.4 (C-1All), 69.7 (C-1$_{linker}$), 68.1 (C-2$_B$), 67.8 (C-2$_A$), 66.4 (C-7$_A$*), 66.2 (C-7$_B$*), 51.3 (C-5$_{linker}$), 31.9 (C-6$_A$*), 31.8 (C-6$_B$*), 28.9 (C-2$_{linker}$), 28.6 (C-4$_{linker}$), 23.3 (C-3$_{linker}$), 20.9 (2 × CH$_3$CO); HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{54}H_{68}N_3O_{13}$, 966.4747; found, 966.4730.

(5-Azido-1-pentyl) 2-*O*-Acetyl-4,7-di-*O*-benzyl-6-deoxy-β-D-*manno*-heptopyranosyl-[1→3]-2-*O*-acetyl-4,7-di-*O*-benzyl-6-deoxy-β-D-*manno*-heptopyranoside (58). To a solution of disaccharide **57** (50 mg, 52 μmol, 1.0 equiv) in a mixture of anhydrous MeOH/DCM (5.2 mL, 1:1 v/v) was added $PdCl_2$ (6.1 mg, 34 μmol, 0.7 equiv). The mixture was stirred for 1 h at 40 °C. After cooling to rt, the solution was diluted with DCM (10 mL) and filtered over Celite. The filtrate was concentrated under reduced pressure and purified by silica gel flash chromatography (PE/EtOAc 10:0 to 7:3) to give **58** (33 mg, 69%): R_f 0.10 (PE/EtOAc 8:2); $[\alpha]_D^{20}$ = −22.4 (c 0.3 $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.32 (m, 20H, CH-Ar), 5.36 (d, J = 3.3 Hz, 1H, H-2$_A$), 5.25 (d, J = 3.3 Hz, 1H, H-2$_B$), 4.93 (d, J = 10.3 Hz, 1H, CHHPh), 4.84 (d, J = 11.1 Hz, 1H, CHHPh), 4.71 (d, J = 11.1 Hz, 1H, CHHPh), 4.67 (d, J = 0.7 Hz, 1H, H-1$_B$), 4.53 (d, J = 12.0 Hz, 1H, CHHPh), 4.49 (d, J = 14.3 Hz, 1H, CHHPh), 4.45 (d, J = 12.0 Hz, 1H, CHHPh), 4.42 (d, J = 14.1 Hz, 1H, CHHPh),

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4.38 (d, J = 10.3 Hz, 1H, CH*H*Ph), 4.25 (d, J = 0.7 Hz, 1H, H-1_A), 3.91−3.85 (m, 2H, H-3_B, H-3_A), 3.72 (td, J = 9.4, 6.3 Hz, 1H, 1a$_{linker}$), 3.65−3.58 (m, 4H, H-7ab$_B$, H-7ab$_A$), 3.51−3.42 (m, 2H, H-5_B, H-4_B), 3.35−3.29 (m, 3H, H-4_A, H-1b$_{linker}$, H-5_A), 3.24 (t, J = 6.9 Hz, 2H, H-5_{linker}), 2.33−2.24 (m, 2H, H-6a$_A$, H-6a$_B$), 2.19 (s, 3H, C*H*$_3$CO), 1.97 (s, 3H, C*H*$_3$CO), 1.86−1.72 (m, 2H, H-6b$_A$, H-6b$_B$), 1.61−1.52 (m, 4H, H-4$_{linker}$, H-2$_{linker}$), 1.40−1.34 (m, 2H, H-3$_{linker}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 170.7 (2 × CO), 138.7−138.3 (4 × C-Ar), 128.7−127.5 (*C*H-Ar), 98.6 (C-1_A), 95.2 (C-1_B), 79.9 (C-4_B), 77.9 (C-3_A), 76.9 (C-4_A), 75.2 (*C*H$_2$Ph), 74.8 (*C*H$_2$Ph), 73.2 (C-3_B), 73.0 (*C*H$_2$Ph), 72.7 (*C*H$_2$Ph), 72.2 (C-5_B), 71.9 (C-5_A), 71.6 (C-2_B), 69.8 (C-1$_{linker}$), 67.8 (C-2_A), 66.5 (C-7_A), 66.3 (C-7_B), 51.4 (C-5_{linker}), 32.0 (C-6_B), 31.9 (C-6_A), 29.1 (C-2$_{linker}$), 28.7 (C-4$_{linker}$), 23.4 (C-3$_{linker}$), 21.3 (2 × *C*H$_3$CO); HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{51}H_{63}N_3O_{13}Na$, 948.4253; found, 948.4253.

(5-Amino-1-pentyl) 2-*O*-Acetyl-6-deoxy-*β*-D-*manno*-heptopyranoside Hydrochloride (1). *Representative Procedure for Pd-Catalyzed Hydrogenation of Monosaccharides.* To a solution of benzylated **55** (11.2 mg, 21.2 μmol, 1.0 equiv) in MeOH (1.1 mL) was added 1 N HCl(aq) (2.1 μL, 1.0 equiv). The solution was degassed with Ar, and Pd black (10 mg) was added. The suspension was stirred under an atmosphere of H_2 at rt for 48 h. The mixture was filtered over Celite to remove the catalyst, and the cake was rinsed with MeOH. The solutions were concentrated under reduced pressure and coevaporated with toluene (3×). The residue was dissolved in distilled H_2O and subjected to C_{18} reversed-phase flash chromatography (H_2O/MeOH 10:0 to 8:2) followed by freeze-drying to give **1** (6.3 mg, 92%) as a white hydroscopic solid. Monosaccharide **1** existed as a mixture of C2/C3 (**1a**/**1b**) regioisomers [ratio **1a**/**1b** ∼ 2.5:1.0 (MeOD); ∼ 1.7:1.0 (D_2O)] resulting from the migration of the acetyl group: $[\alpha]_D^{20}$ = −65.1 (*c* 0.1, MeOH); ^{1}H NMR (400 MHz, MeOD) δ 5.31 (dd, $J_{1,2}$ = 0.9 Hz, $J_{2,3}$ = 3.5 Hz, 1H, H-2 **1a**), 4.68 (dd, $J_{3,4}$ = 9.7 Hz, $J_{2,3}$ = 3.1 Hz, 0.4H, H-3 **1b**), 4.62 (d, $J_{1,2}$ = 0.9 Hz, 1H, H-1 **1a**), 4.54 (d, $J_{1,2}$ = 0.8 Hz, 0.4H, H-1 **1b**), 4.00 (dd, $J_{1,2}$ = 0.8 Hz, $J_{2,3}$ = 3.1 Hz, 0.4H, H-2 **1b**), 3.90−3.80 (m, 1.4H, H-1a$_{linker}$ **1a**/**1b**), 3.77−3.68 (m, 2.8H, H-7ab **1a**/**1b**), 3.65−3.53 (m, 2.8H, H-4 **1b**, H-3 **1a**, H-1b$_{linker}$ **1a**/**1b**), 3.45−3.24 (m, 2.8H, H-4 **1a**/**1b**, H-5 **1a**/**1b**), 2.96−2.89 (m, 2.8H, H-5ab$_{linker}$ **1a**/**1b**), 2.22−2.13 (m, 1.4H, H-6a **1a**/**1b**), 2.12 (s, 1.2H, C*H*$_3$CO **1b**), 2.10 (s, 3H, C*H*$_3$CO **1a**), 1.74−1.58 (m, 7H, H-6b **1a**/**1b**, H-4ab$_{linker}$ **1a**/**1b**, H-2ab$_{linker}$ **1a**/**1b**), 1.54−1.41 (m, 2.8H, H-3ab$_{linker}$ **1a**/**1b**); ^{1}H NMR (500 MHz, D_2O) δ 5.37 (d, $J_{2,3}$ = 3.3 Hz, 1H, H-2 **1a**), 4.85 (dd, $J_{3,4}$ = 9.9 Hz, $J_{2,3}$ = 3.2 Hz, 0.6H, H-3 **1b**), 4.81 (br s, 1H, H-1 **1a**), 4.72 (br s, 1H, H-1 **1b**), 4.13 (d, $J_{2,3}$ = 3.2 Hz, 0.6H, H-2 **1b**), 3.90−3.64 (m, 8H, H-1ab$_{linker}$ **1a**/**1b**, H-3 **1a**, H-4 **1b**, H-7ab **1a**/**1b**), 3.52−3.43 (m, 2.6H, H-4 **1a**/**1b**, H-5 **1a**/**1b**), 3.03−2.97 (m, 3.2H, H-5ab$_{linker}$ **1a**/**1b**), 2.20−2.13 (m, 1.6H, 6a **1a**/**1b**), 2.18 (s, 4.8H, C*H*$_3$CO **1a**/**1b**), 1.77−1.59 (m, 8H, H-6b **1a**/**1b**, H-4ab$_{linker}$ **1a**/**1b**, H-2ab$_{linker}$ **1a**/**1b**), 1.48−1.37 (m, 3.2H, H-3ab$_{linker}$ **1a**/**1b**); ^{13}C NMR (100 MHz, MeOD) δ 172.6 (*C*O **1a**), 172.5 (*C*O **1b**), 101.2 (C-1 **1b**), 100.2 (C-1 **1a**), 77.7 (C-3 **1b**), 74.5 (C-5 **1a**), 74.4 (C-5 **1b**), 73.4 (C-3 **1a**, C-2 **1a**), 72.6 (C-4 **1a**), 70.1 (C-2 **1b**, C-1linker **1a**/**1b**), 69.5 (C-4 **1b**), 59.4 (C-7 **1b**), 59.4 (C-7 **1a**), 40.7 (C-5$_{linker}$ **1a**), 40.6 (C-5$_{linker}$ **1b**), 35.9 (C-6 **1a**), 35.8 (C-6 **1b**), 30.0 (C-2$_{linker}$ **1b**), 29.9 (C-2$_{linker}$ **1a**), 28.2 (C-6 **1a**/**1b**), 24.0 (C-3$_{linker}$ **1a**), 24.0 (C-3$_{linker}$ **1b**), 21.0 (*C*H$_3$CO **1a**/**1b**); MS (ESI-TOF) m/z = 322.4 [M + H]$^+$; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{14}H_{28}NO_7$, 322.1860; found, 322.1863.

(5-Amino-1-pentyl) 2-*O*-Acetyl-6-deoxy-3-*O*-propyl-*β*-D-*manno*-heptopyranoside Hydrochloride (2). Benzylated **54** (13.6 mg, 24.0 μmol, 1.0 equiv) was reacted according to the representative procedure for Pd-catalyzed hydrogenation of monosaccharides and gave **2** (8.3 mg, 95%) as a white hydroscopic solid: $[\alpha]_D^{20}$ = −21.6 (*c* 0.2, MeOH); ^{1}H NMR (400 MHz, MeOD) δ 5.46 (dd, $J_{2,3}$ = 1.5 Hz, $J_{1,2}$ = 1.0 Hz, 1H, H-2), 4.62 (d, $J_{1,2}$ = 1.0 Hz, 1H, H-1), 3.84 (dt, J = 9.7, 6.1 Hz, 1H, H-1a$_{linker}$), 3.75−3.69 (m, 2H, H-7ab), 3.61−3.54 (m, 2H, H-1a$_{Pr}$, H-1b$_{linker}$), 3.43 (dt, J = 8.9, 6.4 Hz, 1H, H-1b$_{Pr}$), 3.38−3.34 (m, 3H, H-3, H-4, H-5), 2.92 (t, J = 7.6 Hz, 2H, H-5ab$_{linker}$), 2.23−2.13 (m, 1H, H-6a), 2.08 (s, 3H, C*H*$_3$CO), 1.71−1.59 (m, 5H, H-6b, H-4ab$_{linker}$, H-2ab$_{linker}$), 1.59−1.52 (m, 2H, H-2ab$_{Pr}$), 1.49−1.42 (m, 2H, H-3ab$_{linker}$), 0.90 (t, J = 7.4 Hz, 3H, H-3$_{Pr}$); ^{1}H NMR (500 MHz, D_2O) δ 5.56 (d, $J_{2,3}$ = 3.1 Hz, 1H, H-2), 4.80 (br s, 1H, H-1), 3.85 (dt, J = 10.1, 6.4 Hz, 1H, H-1a$_{linker}$), 3.81−3.73 (m, 2H, H-7ab), 3.68 (dt, J = 10.1, 6.4 Hz, 1H, H-1b$_{linker}$), 3.65−3.58 (m, 2H, H-1a$_{Pr}$, H-3), 3.53 (dt, J = 9.3, 6.5 Hz, 1H, H-1b$_{Pr}$), 3.49−3.44 (m, 2H, H-4, H-5), 2.22−2.12 (m, 1H, H-6a), 2.18 (s, 3H, C*H*$_3$CO), 1.75−1.51 (m, 7H, H-6b, H-4ab$_{linker}$, H-2ab$_{linker}$, H-2$_{Pr}$), 1.45−1.37 (m, 2H, H-3ab$_{linker}$), 0.87 (t, J = 7.4 Hz, 3H, H-3$_{Pr}$); ^{13}C NMR (100 MHz, MeOD) δ 172.2 (*C*O), 100.2 (C-1), 81.4 (C-3), 74.4 (C-5), 72.6 (C-1$_{Pr}$), 71.5 (C-4), 70.2 (C-1$_{linker}$), 70.0 (C-2), 59.4 (C-7), 40.7 (C-5$_{linker}$), 35.9 (C-6), 30.0 (C-2$_{linker}$), 28.2 (C-4$_{linker}$), 24.1 (C-3$_{linker}$), 24.0 (C-2$_{Pr}$), 20.9 (*C*H$_3$CO), 10.8 (C-3$_{Pr}$); ^{13}C NMR (125 MHz, D_2O) δ 174.0 (*C*O), 99.0 (C-1), 79.8 (C-3), 73.3 (C-5), 72.7 (C-1$_{Pr}$), 70.3 (C-1$_{linker}$, C-4), 69.8 (C-2), 58.4 (C-7), 40.0 (C-5$_{linker}$), 34.1 (C-6), 28.8 (C-2$_{linker}$), 27.0 (C-4$_{linker}$), 22.8 (C-3$_{linker}$, C-2$_{Pr}$), 20.9 (*C*H$_3$CO), 10.3 (C-3$_{Pr}$); MS (ESI-TOF) m/z = 364.5 [M + H]$^+$; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{17}H_{34}NO_7$, 364.2330; found, 364.2333.

(5-Amino-1-pentyl) 2-*O*-Acetyl-6-deoxy-*β*-D-*manno*-heptopyranosyl-[1→3]-2-*O*-acetyl-6-deoxy-*β*-D-*manno*-heptopyranoside Hydrochloride (3). *Representative Procedure for Pd-Catalyzed Hydrogenation of Disaccharides.* A solution of benzylated **58** (14.3 mg, 15.4 μmol) in MeOH (6.0 mL) containing concentrated HCl (1.3 μL, 15.4 μmol, 1.0 equiv) was passed through a 20% $Pd(OH)_2$/C cartridge (CatCart30) using a H-Cube continuous flow hydrogenation system in full-H_2 mode. The temperature was set at 30 °C, and the flow rate was fixed at 1.0 mL·min^{-1}. After one run, the cartridge was rinsed with MeOH (6.0 mL) and then H_2O (6.0 mL). The solutions were concentrated under reduced pressure, and the residue was subjected to C_{18} reversed-phase flash chromatography (H_2O/MeOH 10:0 to 8:2) followed by freeze-drying to give **3** (5.8 mg, 70%) as a white amorphous powder. Disaccharide **3** existed as a mixture of C2/C3 (**3a**/**3b**) regioisomers [ratio **3a**:**3b** ∼ 1.8:1.0 (MeOD); ∼ 1.0:1.0 (D_2O)] resulting from the migration of the C2′ acetyl group: $[\alpha]_D^{20}$ = −2.0 (*c* 0.05 MeOH); ^{1}H NMR of **3a** (400 MHz, MeOD) δ 5.45 (d, $J_{2,3}$ = 3.4 Hz, 1H, H-2$_A$), 5.22 (d, $J_{2,3}$ = 3.4 Hz, 1H, H-2$_B$), 4.77 (br s, 1H, H-1$_B$), 4.62 (br s, 1H, H-1$_A$), 3.90−3.67 (m, 6H, H-1a$_{linker}$, H-3$_B$, H-7ab$_A$, H-7ab$_B$), 3.65−3.55 (m, 2H, H-1b$_{linker}$, H-3$_A$), 3.46−3.29 (m, 4H, H-4$_A$, H-4$_B$, H-5$_A$, H-5$_B$), 2.92 (t, J = 7.5 Hz, 2H, H-5ab$_{linker}$), 2.23−2.07 (m, 2H, H-6a$_A$, H-6a$_B$), 2.10 (s, 3H, C*H*$_3$CO), 2.09 (s, 3H, C*H*$_{3Ac}$), 1.72−1.59 (m, 6H, H-6b$_A$, H-6b$_B$, H-4ab$_{linker}$, H-2ab$_{linker}$), 1.49−1.41 (m, 2H, H-3ab$_{linker}$); ^{13}C NMR of **3a** (100 MHz, MeOD) δ 172.7, 172.2 (2 × *C*O), 100.0 (C-1$_A$), 97.6 (C-1$_B$), 79.9 (C-3$_B$), 74.7, 74.0 (C-5$_A$, C-5$_B$), 73.3 (C-3$_A$), 73.0 (C-2$_B$), 72.4, 70.7 (C-4$_A$, C-4$_B$), 70.4 (C-1$_{linker}$), 70.0 (C-2$_A$), 59.3 (C-7$_A$, C-7$_B$), 40.7 (C-5$_{linker}$), 35.9, 35.7 (C-6$_A$, C-6$_B$), 30.0 (C-2$_{linker}$), 28.2 (C-4$_{linker}$), 24.1 (C-3$_{linker}$), 20.9 (2 × *C*H$_3$CO); HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{23}H_{42}NO_{13}$, 540.2656; found, 540.2649.

(5-Amino-1-pentyl) 2-*O*-Acetyl-6-deoxy-3-*O*-propyl-*β*-D-*manno*-heptopyranosyl-[1→3]-2-*O*-acetyl-6-deoxy-*β*-D-*manno*-heptopyranoside Hydrochloride (4). Benzylated **57** (9.9 mg, 10 μmol, 1.0 equiv) was reacted according to the representative procedure for Pd-catalyzed hydrogenation of disaccharides and gave **4** (3.7 mg, 64%) as a white amorphous powder: $[\alpha]_D^{20}$ = −2.2 (*c* 0.1 MeOH); ^{1}H NMR (400 MHz, MeOD) δ 5.44 (br s, 1H, H-2$_A$), 5.36 (d, $J_{2,3}$ = 2.9 Hz, 1H, H-2$_B$), 4.76 (br s, 1H, H-1$_B$), 4.62 (br s, 1H, H-1$_A$), 3.88−3.77 (m, 2H, H-1a$_{linker}$, H-3$_A$), 3.77−3.68 (m, 4H, H-7ab$_A$, H-7ab$_B$), 3.61−3.52 (m, 2H, H-1b$_{linker}$, H-1a$_{Pr}$), 3.45−3.25 (m, 6H, H-1b$_{Pr}$, H-4$_A$, H-4$_B$, H-5$_A$, H-5$_B$, H-3$_B$), 2.91 (t, J = 7.3 Hz, 2H, H-5ab$_{linker}$), 2.23−2.14 (m, 2H, H-6a$_A$, H-6a$_B$), 2.09 (s, 3H, C*H*$_3$CO), 2.06 (s, 3H, C*H*$_3$CO), 1.71−1.59 (m, 4H, H-4ab$_{linker}$, H-2ab$_{linker}$, H-6b$_A$, H-6b$_B$), 1.59−1.52 (m, 2H, H-2ab$_{Pr}$), 1.49−1.40 (m, 2H, H-3ab$_{linker}$), 0.90 (t, J = 7.3 Hz, 3H, H-3$_{Pr}$); ^{13}C NMR (100 MHz, MeOD) δ 172.8, 171.9 (2 × *C*O), 99.9 (C-1$_A$), 97.6 (C-1$_B$), 81.4 (C-3$_B$), 80.1 (C-3$_A$), 74.7, 74.0 (C-5$_A$, C-5$_B$), 72.6 (C-1$_{Pr}$), 71.3, 70.7 (C-4$_A$, C-4$_B$), 70.4 (C-1$_{linker}$), 70.1 (C-2$_A$), 69.9 (C-2$_B$), 59.3 (C-7$_A$, C-7$_B$), 40.7 (C-5$_{linker}$), 35.7, 35.9 (C-6$_A$, C-6$_B$), 30.0 (C-2$_{linker}$), 28.2 (C-4$_{linker}$), 24.1 (C-3$_{linker}$), 24.0 (C-2$_{Pr}$), 20.9, 20.8 (2 × CH$_3$CO), 10.8 (C-3$_{Pr}$); HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{26}H_{48}NO_{13}$, 582.3126; found, 582.3113.

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■ ASSOCIATED CONTENT

Supporting Information

NMR spectra for all synthetic compounds and HRMS spectra of target heptosides **1**−**4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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