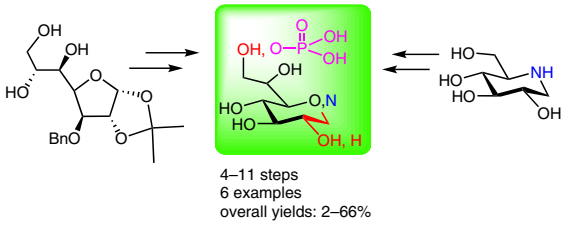
Synthesis M. Blaukopf et al. Feature

Synthesis of 1,5-Anhydro-D-*glycero*-D-*gluco*-heptitol Derivatives as Potential Inhibitors of Bacterial Heptose Biosynthetic Pathways

Markus Blaukopf[a]
Dmytro Atamanyuk[b,1]
Nuno M. Xavier[a,2]
Vincent Gerusz[b,3]
Paul Kosma*[a]

[a] University of Natural Resources and Life Sciences-Vienna, Department of Chemistry, Muthgasse 18, 1190 Vienna, Austria
[b] Mutabilis, Avenue Gaston Roussel, 93230 Romainville, France
paul.kosma@boku.ac.at



Received: 01.09.2017
Accepted after revision: 12.10.2017
Published online: 08.11.2017
DOI: 10.1055/s-0036-1591518; Art ID: ss-2017-z0569-fa

Abstract A series of 1,5-anhydro-D-*glycero*-D-*gluco*-heptitol derivatives have been prepared from 3-*O*-benzyl-1,2-*O*-isopropylidene-D-*glycero*-D-*gluco*-heptofuranose via conversion into anomeric bromide and thiophenyl derivatives, followed by glycal formation and reductive desulfurization, respectively. Global deprotection of the protected intermediates afforded the 1,5-anhydro derivatives of the D-*glycero*-D-*gluco*- and 1,2-dideoxy-D-*altro*- configuration as well as the 1,5-anhydro-2-deoxy-D-*altro*-hept-1-enitol. In addition, the 7-*O*-phosphorylated D-*glycero*-D-*gluco*-heptose and its 1,5-anhydro analogue were prepared in good yields utilizing phosphoramidite chemistry. A novel heptitol analogue based on a 1-deoxynojirimycin scaffold was also elaborated via a Wittig-type chain elongation followed by dihydroxylation, separation of the resulting epimers, and global deprotection. The target compounds, however, were not active as inhibitors of the bacterial sedoheptulose-7-phosphate isomerase GmhA.

Key words heptose, carbohydrates, inhibitor, anhydro-sugar, C6 chain elongation, phosphorylation

A threat to global health is presently associated with the increase of multidrug-resistant bacteria, for several of which common antibiotics are not effective anymore.[4] Novel approaches are therefore urgently needed to identify bacterial targets and to develop appropriate compounds with effective and specific modes of action.[5] Among these targets, the lipopolysaccharide (LPS) of Gram-negative bacteria is of significant importance. LPS is located in the outer membrane of the cell envelope, and harbors non-mammalian, higher-carbon sugars, which fulfill important functions within the bacterial membrane, but are nonetheless involved in a multitude of interactions with components of the innate and adaptive immune system.[6] In structural terms, the LPS may divided into three domains, corresponding to the endotoxic Lipid A, the core region, and the O-antigenic polysaccharide.[7] In addition to LPS, many bacterial surfaces are covered by capsular polysaccharides serving as an additional barrier, which may also contain these higher-carbon sugars as constituents of their repeating units.[8] In particular, the 3-deoxy-D-*manno*-oct-2-ulosonic acid (Kdo) forms the linkage of the inner-core region to the Lipid A anchor and is further extended by several units of L-*glycero*-D-*manno*-heptose (LD-Hep) as well as less frequently by its 6-epimeric form.[9] Moreover, other heptose variants of different configuration and their 6-deoxy derivatives have been found on capsular polysaccharides of important pathogens such as *Campylobacter jejuni*, *Yersinia tuberculosis*, or *Burkholderia pseudomallei*.[10] Recently, both epimeric forms of *glycero*-D-*manno*-heptose linked to serine residues have been identified in bacterial glycoproteins associated with bacterial adhesion.[11]

The biosynthesis of heptoses and their nucleotide-activated forms has been elucidated, starting form sedoheptulose-7-phosphate (**1**), which is isomerized by GmhA[12c] to D-*glycero*-D-*manno*-heptose-7-phosphate (**2**), followed by a kinase step catalyzed by HldE or HddA,[12c] respectively, leading to either the β- or α-anomeric form of the resulting D-*glycero*-D-*manno*-heptose 1,7-bisphosphates **3** and **4**, respectively (Scheme 1).[12] This intermediate has very recently been shown to act as potent inducer of an innate immune response in particular in the context of *Neisseria meningitidis* infections.[13] The biosynthetic pathways diverge from compound **2** leading to the biosynthesis of the unstable ADP-L-*glycero*-β-D-*manno*-heptose (ADP: adenosine 5′-diphosphate) serving as the substrate for the inner-core bacterial heptosyl transferases involved in the assembly of LPS-units (**3** → **5** → **6** → **7**).[14] On the other hand, the glycosyl α-phosphate **4** is converted into the corresponding GDP-D-*glycero*-α-D-*manno* sugar (GDP: guanosine 5′-diphosphate) **9** (**4** → **8** → **9**) involved in the biosynthesis of capsular polysaccharides. The GDP heptose may then undergo further transformations such as deoxygenation and epimerization

(**9** → **10** → **11** or **12**).[10a] The main enzymes involved in these biosynthetic steps have meanwhile been characterized and several crystal structures of the apo-forms and the liganded forms have been published.[15] Blocking these enzymes, which are involved in the early transformations leads, for example, to deep rough type bacterial mutants of the Re chemotype with impaired barrier functions, which are rapidly cleared from serum by the immune system. Heptose-deficient strains from *Escherichia coli*, *Salmonella enterica*, *Shigella flexneri*, *Burkholderia*, and *Neisseria* are known to

Biographical Sketches

Markus Blaukopf obtained his Ph.D. degree in organic chemistry from the University of Natural Resources and Life Sciences, Vienna in 2011 under the supervision of Prof. Paul Kosma. He continued to work in this group for a postdoctoral study on the development of novel potential heptose-based antibacterial agents. Supported by a FWF Schroedinger Fellowship he relocated to Vancouver in 2013 to work on the structure–activity relationship of LPS biosynthetic pathway enzymes in the group of S. G. Withers. In 2015, he returned to the University of Natural Resources and Life Sciences, Vienna where his research activities center around the synthesis of carbohydrate based compounds and their use as glycosyl transferase substrates.

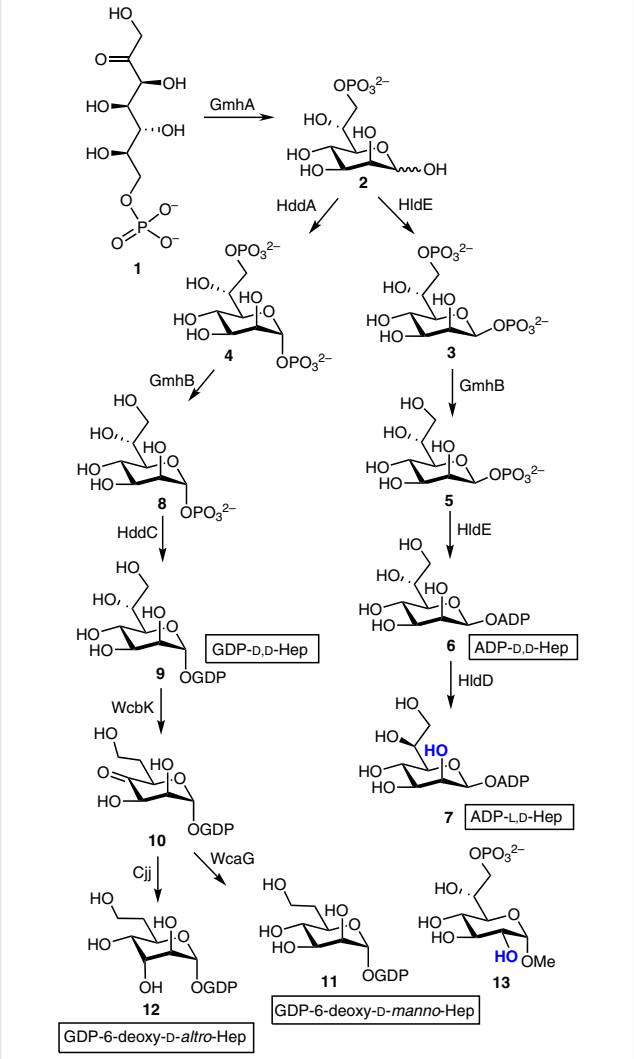
Dmytro Atamanyuk holds a Ph.D. in medicinal chemistry from Lviv National Medical University, Ukraine under the supervision of Prof. Roman Lesyk. He has 9 years of experience in biotech (Mutabilis) and CRO companies (Enamine) in the infectious diseases and oncology as project leader and team leader. Currently he is a project leader in Medicinal Chemistry of AB Science, a Paris-based pharmaceutical company.

Nuno M. Xavier obtained a dual Ph.D. degree in organic chemistry from the University of Lisbon and from the National Institute of Applied Sciences of Lyon in 2011 under the supervision of Prof. Amélia Rauter and Dr. Yves Queneau, respectively. In a postdoctoral study, he worked on the development of novel potential heptose-based antibacterial agents in the group of Paul Kosma at the University of Natural Resources and Life Sciences, Vienna. In 2012, he returned to the University of Lisbon. His research activities – supported by an Investigator Starting Grant from the Portuguese Foundation for Science and Technology (FCT) – are the design and synthesis of original carbohydrate derivatives and nucleoside and nucleotide analogues of biological interest.

Vincent Gerusz holds a Ph.D. degree in chemistry from Stanford University and has 20 years of experience in drug discovery in both large pharmaceutical and biotech companies. He has led various research teams and is co-inventor of several NCEs put in development in the fields of infectious diseases and oncology. Currently he is heading the Medicinal Chemistry of Debiopharm, a Swiss-based global biopharmaceutical group.

Paul Kosma obtained a Ph.D. degree in organic chemistry at the University of Technology in Vienna. Ensuing postdoctoral experience was obtained at the SANDOZ-research Institute in Vienna and the N. D. Zelinsky Institute of Organic Chemistry in Moscow. Since 1992 he holds a chair of Organic Chemistry at the University of Natural Resources and Life Sciences, Vienna. His main research interests are focused on the synthesis of nucleotide-activated sugars, triterpene glycosides, and complex glycans related to biomedically relevant cell-surface glycans from bacteria, parasites, and viruses.

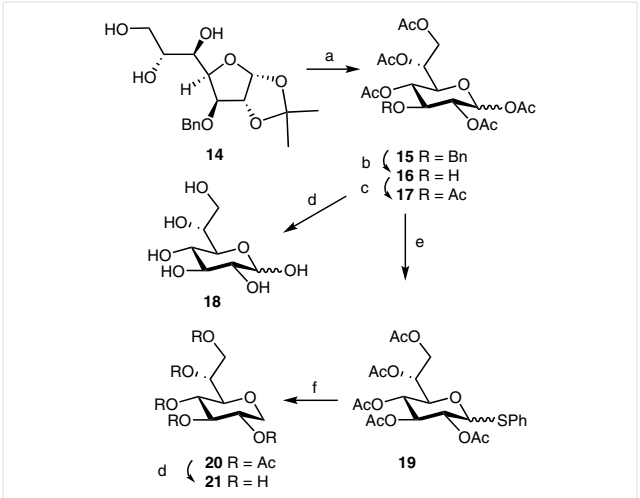
be avirulent.[16] As a consequence, suitable inhibitors of the heptose biosynthetic pathways hold promise as broad-band drug candidates, which would not harm mammalian enzymes, would not damage the gut microbiome, and could serve as potent antivirulence agents.[5a]



Scheme 1 Biosynthesis of nucleotide-activated heptoses and GmhA inhibitor **13**

Inhibition of the first enzymatic steps catalyzed by the sedoheptulose-7-phosphate isomerase GmhA and anomeric kinases HldE and HddA, respectively, would affect both biosynthetic pathways involved in LPS and CPS (capsular polysaccharide) assembly.[17] Previously, the group of Vincent has carried out the preparation of a library of D-*glycero*-D-*manno*-heptose 7-phosphates with manifold structural variations at the exocyclic side chain.[18] Notably the 2-epimeric derivative **13**, corresponding to a D-*gluco*-configured D-*glycero*-heptose-7-phosphate, was found to inhibit both GmhA and HldE with IC_{50} values in the low micromolar range. In order to further investigate the impact of an equatorial 2-hydroxy group, we have set out to prepare additional D-*glycero*-D-*gluco*- derivatives with modifications in the vicinity of the anomeric center, including 1-deoxy derivatives, which were also envisaged to potentially inhibit the ensuing kinase reactions HldE and HddA, respectively. Furthermore, the biological activity of related analogues obtained by replacement of the ring oxygen by nitrogen should also be evaluated.

The syntheses of the target compounds were based on transformations starting from known 3-*O*-benzyl-1,2-*O*-isopropylidene-D-*glycero*-α-D-*gluco*-heptofuranose (**14**).[19] Acid hydrolysis of the acetal group using 50% aqueous TFA followed by per-O-acetylation afforded the penta-*O*-acetyl derivative **15** in 73% yield (Scheme 2). The coupling constant $J_{5,6}$ (3.0 Hz) was in agreement with related derivatives of D-*glycero*-D-*manno*-heptose, thereby securing the assignment of the D-*glycero*-configuration at C-6.[20] Compound **15** was subjected to hydrogenation on Pd/C to give the alcohol **16** in 92% yield. Compound **16** was fully deprotected via Zemplén transesterification to give the D-*glycero*-D-*gluco*-heptose **18** in nearly theoretical yield as 1:1.9 α,β-anomeric mixture.[19]

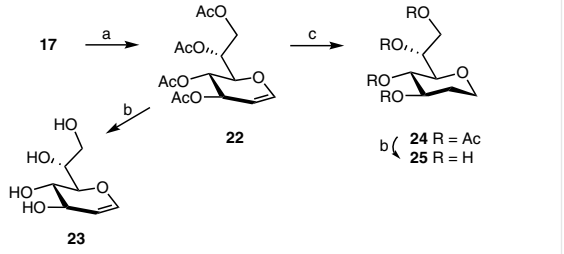


Scheme 2 Synthesis of 1-deoxy derivatives. *Reagents and conditions*: (a) 50% aq TFA, 16 h, r.t., 16 h, then Ac_2O, pyr, r.t., 12 h, 73%; (b) H-cube, 10% Pd/C, MeOH, r.t., 92%; (c) Ac_2O, pyr, DMAP, r.t., 12 h, 97%; (d) 0.1 M NaOMe, MeOH, r.t., quant. for **18**, 92% for **21**; (e) thiophenol, $BF_3{\cdot}OEt_2$, CH_2Cl_2, r.t., 12 h, 43%; (f) H-cube, Raney-nickel, EtOH, 40 °C, 55%.

Prior to the preparation of the 1-deoxy derivatives, alcohol **16** was converted into the per-O-acetylated heptose **17** in 97% yield. Introduction of the phenyl-1-thio group was achieved in a moderate yield by reaction of **17** with thiophenol in the presence of $SnCl_4$ as Lewis acid promoter. The reaction could not be forced for full conversion, since only the β-anomeric acetate was reactive, while unreacted α-anomer could be recovered from the reaction mixture in 39% yield. Subsequently, reductive desulfurization[21] of the

thioglycoside **19** was accomplished by hydrogenation with Raney-nickel under microfluidic conditions for an extended reaction time (32 h) at 40 °C, to give **20** in 55% yield. Its subsequent de-O-acetylation produced the 1,5-anhydro compound **21** in 92% yield.

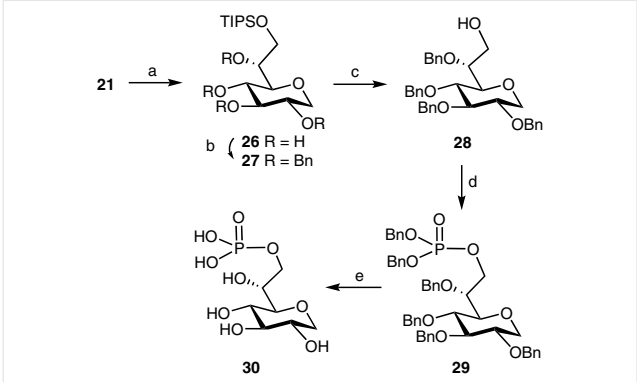
Next, 1,2-dideoxy derivatives were generated from glycal **22**, prepared in 75% yield via conversion of **17** into the corresponding anomeric bromide by treatment with HBr in acetic acid, followed by elimination using zinc in buffered acetic acid (Scheme 3). Glycal **22** was deprotected to furnish tetraol glycal **23** in 90% yield. In addition, the double bond was hydrogenated to afford the 1,2-dideoxy derivative **24** in 85% yield followed by Zemplén de-O-acetylation to give **25** in 98% yield.



Scheme 3 Synthesis of 1,2-dideoxy derivatives. *Reagents and conditions*: (a) 33% HBr/AcOH, then NaOAc, Zn dust, AcOH, sonication, 0 °C, 30 min, 75%; (b) 0.1 M NaOMe, MeOH, r.t., 90% for **23**, 98% for **25**; (c) 10% Pd/C, H_2, THF, r.t., 12 h, 85%.

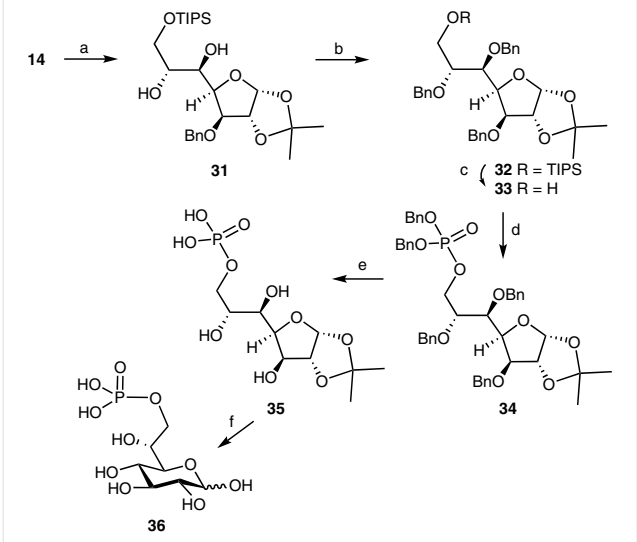
Proceeding toward the 7-O-phosphorylated derivatives, the 1,5-anhydro derivative **21** was converted into the 7-*O*-triisopropylsilyl derivative **26** by reaction with TIPS-chloride/imidazole in THF in modest yield followed by benzylation with NaH/benzyl bromide in DMF, which gave the tetra-*O*-benzyl derivative **27** in 54% yield (Scheme 4). Next, the TIPS ether was smoothly cleaved by the action of TBAF to produce the primary alcohol **28** in 82% yield, which was then subjected to phosphoramidite-based phosphitylation with ensuing oxidation by *m*CPBA to give phosphotriester **29** in 85% yield.[22] De-O-benzylation of **29** by hydrogenolysis on Pd/C gave the 7-*O*-phosphorylated 1,5-anhydro-D-*glycero*-D-*gluco*-derivative **30** in near quantitative yield.

Along similar lines, albeit in improved yields, compound **14** was converted into the reducing D-*glycero*-D-*gluco*-heptose 7-*O*-phosphate **36**. Regioselective silylation at position 7 by reaction with TIPS-chloride in THF/DABCO gave triisopropylsilyl derivative **31** in 71% yield (Scheme 5). To selectively address the primary alcohol for phosphorylation, the remaining hydroxyl groups were benzylated. Similar to **27**, compound **32** was isolated in only 44% yield, when basic conditions (NaH and BnBr in DMF) were used, due to the base lability of the silyl ether group. The yield, however, could be considerably improved (85%) using benzyl trichloroacetimidate[23] in the presence of triflic acid. Cleavage of



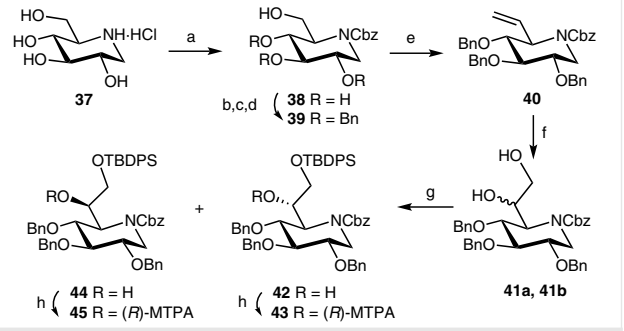
Scheme 4 Synthesis of 7-*O*-phosphono-1-deoxy derivatives. *Reagents and conditions*: (a) TIPSCl, imidazole, THF, r.t., 32%, (b) NaH, BnBr, DMF, r.t., 16.5 h, 54%; (c) TBAF, THF, r.t., 17 h, 82%; (d) $(BnO)_2PN(i\text{-}Pr)_2$, 1*H*-tetrazole, CH_2Cl_2, r.t., then −78 °C, *m*CPBA, 1 h, 85%; (e) H_2, 10% Pd/C, r.t., aq EtOH/AcOH, 99%.

the TIPS ether was carried out by the action of TBAF to produce the primary alcohol **33** in 60% yield. The ensuing phosphorylation of **33** with *N*,*N*-diisopropyl-di-*O*-benzylphosphorane in the presence of 1*H*-tetrazole afforded the intermediate phosphite-triester which was then oxidized with *m*CPBA to give the phosphotriester derivative **34** in 78% yield. Deprotection of **34** was performed in two steps by first removing the benzyl protecting groups by hydrogenolysis in the presence of Pd/C giving **35**, followed by cleavage of the 1,2-acetonide by the action of 10% aqueous TFA to provide the 7-*O*-phosphoryl-D-*glycero*-D-*gluco*-heptose derivative **36** in 99% yield (Scheme 5).



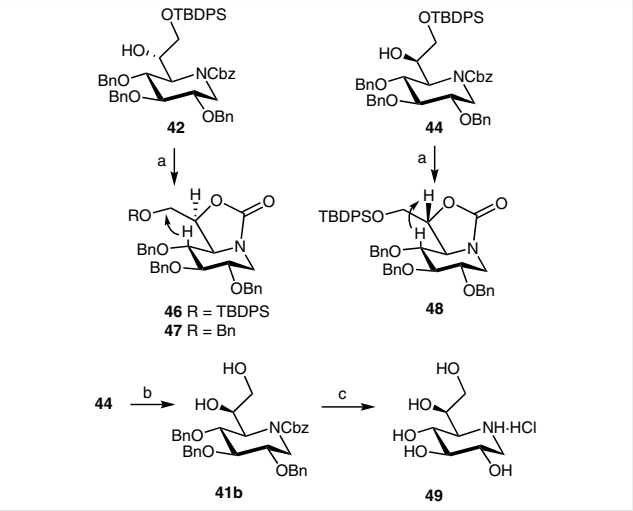
Scheme 5 Synthesis of D-*glycero*-D-*gluco*-heptose 7-phosphate. *Reagents and conditions*: (a) TIPSCl, DABCO, THF, r.t., 71%, (b) TfOH, Bn-trichloroacetimidate, CH_2Cl_2, 0 °C, 85% (c) TBAF, THF, r.t., 5 h, 60%; (d) $(BnO)_2PN(i\text{-}Pr)_2$, 1*H*-tetrazole, CH_2Cl_2, r.t., then −78 °C, *m*CPBA, 0.5 h, 78%; (e) H_2, 10% Pd/C, r.t., aq EtOH/AcOH, 99%.

For the synthesis of the 5-iminoheptitol derivative **49**, 1-deoxynojirimycin hydrochloride (**37**) was used as a starting material and first protected as the known *N*-Cbz derivative **38** (Scheme 6).[24] In order to address carbon 6 for chain elongation, the primary alcohol group was converted into the 6-*O*-dimethoxytrityl derivative followed by per-O-benzylation and acidic hydrolysis of the DMTr protecting group to **39** in 57% yield (three steps). For the intended preferential formation of the D-*glycero*-configured compound, Wittig olefination of an intermediate 6-aldehyde – obtained via Swern oxidation of **39** – followed by catalytic dihydroxylation according to Kishi's rule was carried out.[25] Reaction of the aldehyde with methyl triphenylphosphonium bromide/*n*-BuLi gave olefin **40** in 62% yield (2 steps). Catalytic osmylation then afforded an excellent yield of the diols **41a** and **41b**, albeit in poor diastereoselectivity (1.6:1),[26] presumably due to steric congestion exerted by the *N*-benzyloxycarbonyl appendix. A similar low diastereoselectivity (2:1 ratio) has previously been observed for dihydroxylation of a Boc-protected 1-deoxy-*manno*-nojirimycin derivative.[27]



Scheme 6 Synthesis of iminoheptitols. *Reagents and conditions*: (a) CbzCl, $NaHCO_3$, aq MeOH, 67%; (b) DMTrCl, DMAP, pyr; (c) BnBr, NaH, DMF; (d) 80% aq AcOH, 57% (3 steps); (e) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, –70 °C, then PPh_3MeBr, *n*-BuLi, THF, –60 °C to r.t., 62% (2 steps); (f) cat. OsO_4, NMO, aq THF, 97%; (g) TBDPSCl, imidazole, CH_2Cl_2; 95%; (h) (*S*)-MPTA, cat. DMAP, CCl_4, pyr; 38% for **43**, 25% for **45**.

Separation of the isomers had to rely on a regioselective 7-O-silylation to produce the 7-*O*-TBDPS derivatives **42** and **44** in a combined 95% yield. Assignment of the new stereocenter at C-6 was not straightforward – complicated by the presence of Cbz-rotamers – and was first tried upon formation of the (*R*)-MPTA Mosher ester derivatives **43** and **45**.[28] In order to overcome severe line broadening, NMR spectra had to be recorded in toluene-d_8 at 75 °C. Minor differences in the chemical shift data and the presence of rotamers (**42**: H-5 at 4.45, H-6 at 5.92 ppm, **44**: H-5 at 4.59 and 4.54, H-6 at 5.84 and 5.80 ppm) did not allow for an unambiguous assignment of the stereochemistry at C-6. A conclusive assignment, however, could be achieved upon formation of the bicyclic derivatives **46**–**48**, respectively. Attempted benzylation of **42** with NaH/benzyl bromide in DMF furnished the 7-*O*-silyl ether **46** in 38% yield and the perbenzylated carbamate **47** in 47% yield with concomitant loss of the benzyloxy protecting group (Scheme 7). Facile formation of the 1,3-oxazolidinone ring from Cbz-carbamates under basic conditions has previously been described.[29] NOESY experiments recorded for **47** and **48** in $CDCl_3$ and benzene-d_6, respectively, showed the interaction between H-4 and H-7 in compound **47** versus H-4 and H-6 in compound **48**, thus establishing the D-*glycero* configuration of the major isomer **42** and the L-*glycero* form for the minor isomer **44**.



Scheme 7 Assignment of the stereochemistry at C-6 and deprotection. *Reagents and conditions*: a) BnBr, NaH, DMF, 38% for **46**, 47% for **47**; 37% for **48**; b) HF·pyr, THF, 98%; c) H_2, Pd/C, THF , then aq 1 M HCl, 52%.

Deprotection was performed for **44** and comprised removal of the 6-*O*-TBDPS group with HF-pyridine, which gave **41b** in near theoretical yield. Hydrogenolysis of the Cbz and benzyl was not straightforward and THF had to be used as solvent, since the reaction in methanol led to formation of the corresponding *N*-methyl derivative. The resulting amine was converted into the hydrochloride form followed by desalting on Sephadex G-10 to give **49** in 52% yield. The stereochemical assignment of both 6-epimers was further substantiated by the chemical shift of C-6 for the L-*glycero* isomer **49** (69.8 ppm), which is consistent with previously published NMR data of the related L-*glycero*-D-*manno*-heptose derivative[20] as well as 1,5-dideoxy-1,5-imino-*glycero*-D-*manno*-heptitol derivatives.[27,30]

The inhibitory properties of compounds **21**, **23**, **25**, **30**, **36**, and **49** were tested according to the literature.[31] None of the compounds, however, acted as effective inhibitors, thus substantiating the importance of the anomeric hydroxyl group for the interaction with GmhA. Compound **49**, however, is also of interest as a potential glycosidase inhibitor[32] complementing the previously prepared series of 1,5-dideoxy-1,5-iminoheptitols of the L- and D-*glycero*-D-*manno*-, L-

glycero-D-*altro*- and D-*glycero*-L-*gulo*- configuration.[27,30,33] The synthesis and activity of more potent inhibitors targeting the Zn-ion of GmhA will be published in due course.

All purchased chemicals were used without further purification, unless stated otherwise. The promotor $BF_3{\cdot}OEt_2$ was used as a solution in Et_2O (≥46% according to the manufacturer). Solvents were dried over activated 3Å (acetone, Et_2O) or 4Å (CH_2Cl_2, DMF, pyridine) molecular sieves. Anhyd MeOH (Merck) and anhyd THF (Sigma-Aldrich) were purchased. Cation exchange resin DOWEX 50 H^+ was regenerated by consecutive washing with HCl (3 M), H_2O, and anhyd MeOH. Aqueous solutions of salts were saturated unless stated otherwise. Concentration of organic solutions was performed under reduced pressure <40 °C. Optical rotations were measured with a PerkinElmer 243 B Polarimeter. $[\alpha]_D^{20}$ values are given in units of 10^{-1} deg·cm^2·g^{-1}. TLC was performed on Merck precoated plates: generally on 5 × 10 cm, layer thickness 0.25 mm, Silica Gel $60F_{254}$; alternatively on HPTLC plates with 2.5 cm concentration zone (Merck). Spots were detected by dipping reagent (anisaldehyde/H_2SO_4) or 5% ethanolic phosphomolybdic acid. For column chromatography silica gel (0.040–0.063 mm) was used. HP-column chromatography was performed on pre-packed columns (YMC-Pack SIL-06, 0.005 mm, 250 × 10 mm and 250 × 20 mm). Desalting after ester saponification was performed on pre-packed PD-10 columns (GE Healthcare, Sephadex™ G-25 M). NMR spectra were recorded with Bruker Avance III 300, 400 and 600 instruments using standard Bruker NMR software. ^{1}H spectra were referenced to 7.26 ($CDCl_3$) and 0.00 (D_2O, external calibration to 2,2-dimethyl-2-silapentane-5-sulfonic acid) ppm unless stated otherwise. ^{13}C spectra were referenced to 77.00 ($CDCl_3$), 49.00 (CD_3OD) and 67.40 (D_2O, external calibration to 1,4-dioxane) ppm. ^{31}P spectra were referenced to 0.00 ppm (orthophosphoric acid) for solutions in D_2O and according to ref.[34] for solutions in $CDCl_3$. ESI-MS data were obtained on a Waters Micromass Q-TOF Ultima Global instrument.

1,2,4,6,7-Penta-*O*-acetyl-3-*O*-benzyl-D-*glycero*-D-*gluco*-heptopyranose (15)

A solution of **14** (583 mg, 1.71 mmol) in 50% aq TFA (10 mL) was stirred at r.t. for 16 h. The reaction mixture was concentrated and co-evaporated with toluene (3 × 10 mL). The remaining slightly red oil was taken up in pyridine (4 mL), cooled to 0 °C, and Ac_2O (4 mL) was added dropwise at 0 °C. The mixture was stirred at r.t. for 12 h, then cooled to 0 °C, and MeOH (5 mL) was added dropwise. The mixture was then diluted with $CHCl_3$ (15 mL), sat. aq $NaHCO_3$ (10 mL) was added, and stirred for 15 min. The layers were separated, the aqueous layer was reextracted with $CHCl_3$ (10 mL) and the combined organic layers were dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (eluent: hexane/EtOAc, 3:1 → EtOAc) to afford the title compound **15** (645 mg, 73%) as a colorless amorphous solid.

^{1}H NMR (600 MHz, $CDCl_3$): δ (α anomer) = 7.36–7.21 (m, 5 H, ArH), 6.29 (d, $J_{1,2}$ = 3.5 Hz, 1 H, H-1), 5.13 (t, $J_{4,3}$ = $J_{4,5}$ = 9.8 Hz, 1 H, H-4), 5.15–5.09 (m, 1 H, H-6), 5.00 (dd, $J_{2,3}$ = 9.9 Hz, $J_{1,2}$ = 3.5 Hz, 1 H, H-2), 4.68 (d, J= 11.8 Hz, 1 H, C*H*$_2$Ph), 4.60 (d, J = 11.8 Hz, 1 H, C*H*$_2$Ph), 4.32 (dd, $J_{7a,7b}$ = 12.0 Hz, $J_{7a,6}$ = 3.9 Hz, 1 H, H-7a), 4.20 (dd, $J_{7b,6}$ = 7.5 Hz, 1 H, H-7b), 4.04 (dd, $J_{5,6}$ = 2.5 Hz, $J_{4,5}$ =10.5 Hz, 1 H, H-5), 3.92 (app t, J = 9.6 Hz, H-3), 2.14, 2.06, 2.04, 2.01, 1.98 (5 s, each 3 H, CH_3).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.09, 169.58, 169.56, 169.07 (C=O), 128.46, 127.88, 127.56 (ArCH), 89.23 (C-1), 77.2 (C-3), 74.84 (*C*H$_2$Ph), 71.71 (C-5), 71.32, 69.91, 69.83 (C-2, C-4, C-6), 61.27 (C-7), 20.90–20.67 (5 × CH_3).

^{1}H NMR for (600 MHz, $CDCl_3$): δ (β anomer) = 7.36–7.21 (m, 5 H, ArH), 5.61 (d, $J_{1,2}$ = 7.9 Hz, 1 H, H-1), 5.16–5.08 (m, 3 H, H-2, H-4, H-6), 4.60 (s, 2 H, C*H*$_2$Ph), 4.29 (dd, $J_{7a,6}$ = 4.0 Hz, $J_{7a,7b}$ = 12.0 Hz, 1 H, H-7a), 4.25 (dd, $J_{7b,6}$ = 7.1 Hz, $J_{7a,7b}$ = 12.0 Hz, 1 H, H-7b), 3.77 (dd, $J_{5,6}$ = 2.9 Hz, $J_{4,5}$ = 9.8 Hz, 1 H, H-5), 3.71 (t, $J_{3,4}$ = $J_{2,3}$ = 8.9 Hz, 1 H, H-3), 2.10, 2.07, 2.05, 2.02, 1.97 (5 s, each 3 H, CH_3).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.09, 169.58, 169.56, 169.07 (C=O), 128.51, 127.98, 127.84 (ArCH), 92.00 (C-1), 79.88 (C-3), 74.39 (C-5), 74.21 (*C*H$_2$Ph), 71.36 (C-2), 69.85, 69.83 (C-4, C-6), 61.25 (C-7), 20.90, 20.84, 20.78, 20.72, 20.67 (5 × CH_3).

HRMS (ESI): m/z [M + COOH]$^+$ calcd for $C_{25}H_{31}O_{14}$: 555.1719; found: 555.1714.

1,2,4,6,7-Penta-*O*-acetyl-D-*glycero*-D-*gluco*-heptopyranose (16)

A solution of **15** (50 mg, 0.098 mmol) in MeOH (33 mL) was hydrogenated in an H-Cube (H-Cube SS, cartridge Pd/C 10%, 33 mm, flow rate 0.2 mL/min, H_2 mode: full) at 25 °C. The column was washed with 10 mL MeOH until no more product was detectable by TLC. After one run, TLC indicated complete consumption of the starting material. Evaporation of the solution gave 40 mg of crude product, which was purified by flash chromatography (toluene/EtOAc, 1:1) to give 38 mg (92%) of product **16** as a syrup.

^{1}H NMR (600 MHz, $CDCl_3$): δ (α anomer) = 6.29 (d, $J_{1,2}$ = 3.7 Hz, 1 H, H-1), 5.21–5.17 (m, 1 H, H-6), 5.07–5.00 (m, 1 H, H-4), 4.94 (dd, $J_{2,3}$ = 10.5 Hz, 1 H, H-2), 4.36 (dd, $J_{7a,7b}$ = 12.0 Hz, $J_{7a,6}$ = 3.9 Hz, 1 H, H-7a), 4.17 (dd, $J_{7b,6}$ = 7.4 Hz, 1 H, H-7b), 4.09 (dd, $J_{5,4}$ = 10.4 Hz, $J_{5,6}$ = 2.4 Hz, 1 H, H-5), 4.01 (t, $J_{3,4}$ = 9.6 Hz, 1 H, H-3), 2.18, 2.14, 2.09, 2.08, 2.05 (5 s, each 3 H, CH_3).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.73–170.01 (q, 5 × C=O), 89.11 (C-1), 71.63 (C-2), 71.28 (C-4), 71.16 (C-5), 70.17 (C-3), 69.89 (C-6), 61.51 (C-7), 20.91–20.56 (5 × CH_3).

^{1}H NMR (600 MHz, $CDCl_3$): δ (β anomer) = 5.63 (d, $J_{1,2}$ = 8.2 Hz, 1 H, H-1), 5.21–5.17 (m, 1 H, H-6), 5.07–5.00 (m, 1 H, H-4), 4.97 (dd, $J_{2,3}$ = 9.3 Hz, $J_{1,2}$ = 8.2 Hz, 1 H, H-2), 4.32 (dd, $J_{7a,7b}$ = 12.0 Hz, $J_{7a,6}$ = 4.0 Hz, 1 H, H-7a), 4.21 (dd, $J_{7b,6}$ = 7.2 Hz, 1 H, H-7b), 3.80 (dd, $J_{5,4}$ = 10.0 Hz, $J_{5,6}$ = 2.8 Hz, 1 H, H-5), 3.74 (t, $J_{3,4}$ = 9.3 Hz, 1 H, H-3), 2.16, 2.12, 2.10, 2.09, 2.05 (5 s, each 3 H, CH_3).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.73–170.01 (q, 5 × C=O), 91.69 (C-1), 73.99 (C-5), 73.88 (C-3), 72.68 (C-2), 71.28 (C-4), 69.75 (C-6), 61.44 (C-7), 20.91–20.56 (5 × CH_3).

HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{17}H_{24}O_{12}Na$: 443.1160; found: 443.1156.

D-*Glycero*-D-*gluco*-heptose (18)

A solution of **16** (38 mg, 0.09 mmol) in MeOH (3 mL) was stirred with 0.1 M NaOMe (0.2 mL) for 12 h at r.t. The solution was made neutral by adding Dowex 50 H^+ resin, filtered, and the filtrate was concentrated. The residue was passed over a PD-10 column and eluted with HPLC-grade H_2O. The eluate was lyophilized to give 19 mg (quant.) of **18** as an amorphous solid; $[\alpha]_D^{20}$ –47.2 (*c* 0.26, H_2O).

^{1}H NMR (600 MHz, D_2O): δ = 5.16 (d, $J_{1,2}$ = 3.7 Hz, H-1α), 4.56 (d, $J_{1,2}$ = 7.9 Hz, H-1β), 3.96–3.94 (m, 1 H, H-6), 3.86 (dd, $J_{5,4}$ = 10.1 Hz, $J_{5,6}$ = 2.3 Hz, H-5α), 3.74 (dd, $J_{7a,7b}$ = 11.9 Hz, $J_{7a,6}$ = 3.1 Hz, 1 H, H-7a), 3.66 (dd, $J_{7b,6}$ = 7.4 Hz, 1 H, H-7b), 3.65 (app t, H-3α), 3.52–3.44 (m, H-2α, H-5β, H-4α), 3.42 (dd, $J_{3,4}$ = 9.1 Hz, H-3β), 3.18 (app t, $J_{2,3}$ = 8.9 Hz, H-2β).

^{13}C NMR (150 MHz, D_2O): δ (α anomer) = 92.80 (C-1), 73.81 (C-3), 72.68 (C-6), 72.08 (C-5), 71.16 (2 C, C-2, C-4), 62.68 (C-7).

^{13}C NMR (150 MHz, D_2O): δ (β anomer) = 96.91 (C-1), 77.00 (C-5), 76.74 (C-3), 74.78 (C-2), 72.49 (C-6), 71.16 (C-4), 62.43 (C-7).

HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_7H_{14}O_7$: 209.0667; found: 209.0665.

1,2,3,4,6,7-Hexa-*O*-acetyl-D-*glycero*-D-*gluco*-heptopyranose (17)

Compound **15** (633 mg, 1.24 mmol) was dissolved in MeOH (24 mL) and hydrogenated in an H-Cube for 12 h (H-Cube SS; cartridge: 10% Pd/C 33 mm; solvent: MeOH; flow rate: 0.2 mL; H_2-mode: full; temperature: 50 °C). The reaction mixture was concentrated (540 mg) and dissolved in pyridine (2 mL). Ac_2O (0.5 mL) and a catalytic amount of DMAP were added and the mixture was stirred at r.t. for 12 h. The mixture was cooled to 0 °C, MeOH (1 mL) was added, stirred for 10 min, and then diluted with CH_2Cl_2 (5 mL). The organic phase was washed with sat aq $NaHCO_3$ (2 × 5 mL), dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography (toluene/EtOAc, 4:1 → 1:1) to give compound **16** (557 mg, 1.20 mmol, 97%) as a colorless amorphous solid. The reaction mixture was evaporated to dryness (540 mg), taken up in pyridine (2 ml), Ac_2O (500 µl), a catalytic amount of DMAP and the reaction was stirred at room temperature for 12h. The reaction mixture was cooled to 0°C, MeOH (1 ml) was added and the reaction mixture was stirred for 10 minutes, diluted with DCM (5 ml), washed with sat. aqu. $NaHCO_3$ (2 × 5 ml), dried ($MgSO_4$), evaporated to dryness and directly purified *via* column chromatography (silica gel 60, T/EtOAc4/1 ->T/EE 1/1), to give the title compound **17** (557 mg, 1.20 mmol, 97%) as white solid.

^{1}H NMR (600 MHz, $CDCl_3$): δ (α anomer) = 6.31 (d, $J_{1,2}$ = 3.7 Hz, 1 H, H-1), 5.43 (t, J = 9.6 Hz, 1 H, H-3), 5.18–5.15 (m, 2 H, H-4, H-6), 5.04 (dd, $J_{1,2}$ = 3.7 Hz, $J_{2,3}$ = 10.6 Hz, 1 H, H-2), 4.32 (dd, $J_{7a,6}$ = 4.3 Hz, $J_{7a,7b}$ = 12.0 Hz, 1 H, H-7a), 4.16 (dd, $J_{5,4}$ = 10.5 Hz, $J_{5,6}$ = 2.8 Hz, 1 H, H-5), 4.14 (dd, $J_{7b,6}$ = 7.1 Hz, 1 H, H-7b), 2.17, 2.16, 2.08, 2.08, 2.05, 2.02 (6 s, each 3 H, 6 × CH_3).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 88.78 (C-1), 70.96 (C-5), 69.92 (C-3), 69.75 (C-6), 69.01 (C-2), 68.81 (C-4), 61.38 (C-7), 20.85–20.51 (6 × CH_3).

^{1}H NMR (600 MHz, $CDCl_3$): δ (β anomer) = 5.68 (d, $J_{1,2}$ = 8.1 Hz, 1 H, H-1), 5.21 (t, $J_{3,2}$ = $J_{3,4}$ = 9.2 Hz, 1 H, H-3), 5.18–5.15 (m, 1 H, H-6), 5.13 (app t, J = 9.6 Hz, 1 H, H-4), 5.08 (dd, $J_{1,2}$ = 8.4 Hz, $J_{2,3}$ = 9.1 Hz, 1 H, H-2), 4.29 (dd, $J_{7a,6}$ = 4.3 Hz, $J_{7a,7b}$ = 11.9 Hz, 1 H, H-7a), 4.19 (dd, $J_{7b,6}$ = 7.0 Hz, 1 H, H-7b), 3.88 (dd, $J_{5,4}$ = 9.9 Hz, $J_{5,6}$ = 3.1 Hz, 1 H, H-5), 2.11, 2.08, 2.07, 2.05, 2.03, 2.01 (6 s, each 3 H, 6 × CH_3).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 91.69 (C-1), 73.87 (C-5), 72.79 (C-3), 70.05 (C-2), 69.65 (C-6), 68.78 (C4), 61.28 (C-7), 20.85–20.51 (6 × CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{26}O_{13}SNa$: 485.1266; found: 485.1268.

Phenyl 2,3,4,6,7-Penta-*O*-acetyl-1-thio-D-*glycero*-α,β-D-*gluco*-heptopyranoside (19)

A solution of **17** (557 mg, 1.20 mmol) in anhyd CH_2Cl_2 (5 mL) was stirred under argon at 0 °C. Thiophenol (143 µL, 1.20 mmol) was added followed by dropwise addition of a 1 M solution of $SnCl_4$ in CH_2Cl_2 (663 µL) and the solution was stirred at r.t. for 12 h. The reaction mixture was diluted with CH_2Cl_2 (5 mL), washed with sat. aq $NaHCO_3$ (5 mL) and the aqueous phase was reextracted with CH_2Cl_2 (5 mL). The combined organic phases were dried ($MgSO_4$), concentrated, and the residue was purified by column chromatography (toluene/EtOAc, 7:1) to afford an anomeric mixture (α/β = 1:2) of **19** (266 mg, 0.51 mmol, 43%) as a colorless oil; R_f = 0.65 (EtOAc/hexane, 1:1).

^{1}H NMR (600 MHz, $CDCl_3$): δ (α anomer) = 7.51–7.15 (m, 5 H, ArH), 6.27 (d, $J_{1,2}$ = 4.1 Hz, 1 H, H-1), 5.51 (t, $J_{3,2}$ = $J_{3,4}$ = 9.6 Hz, 1 H, H-3), 5.23–5.20 (m, 1 H, H-6), 5.19–5.17 (m, 1 H, H-4), 4.96 (dd, $J_{1,2}$ = 4.0 Hz, $J_{2,3}$ = 10.3 Hz, 1 H, H-2), 4.35 (dd, $J_{5,4}$ = 10.4 Hz, $J_{5,6}$ = 2.3 Hz, 1 H, H-5), 4.29 (dd, $J_{7a,6}$ = 4.6 Hz, $J_{7a,7b}$ = 12.0 Hz, 1 H, H-7a), 4.17 (dd, $J_{7b,6}$ = 7.2 Hz, 1 H, H-7b), 2.09 (s, 9 H), 2.06 (s, 3 H), 2.03 (5 s, each 3 H, 5 × CH_3).

^{1}H NMR (600 MHz, $CDCl_3$): δ (β anomer) = 7.51–7.15 (m, 5 H, ArH), 5.20–5.13 (m, 2 H, H-3, H-6), 5.04 (t, $J_{4,3}$ ≅ $J_{4,5}$ = 10.0 Hz, 1 H, H-4), 4.92 (app t, $J_{2,1}$ = 10.0 Hz, $J_{2,3}$ = 9.6 Hz, 1 H, H-2), 4.64 (d, $J_{1,2}$ = 10.0 Hz, 1 H, H-1), 4.32 (dd, $J_{7a,6}$ = 4.2 Hz, $J_{7a,7b}$ = 11.8 Hz, 1 H, H-7a), 4.21 (dd, $J_{7b,6}$ = 7.2 Hz, 1 H, H-7b), 3.74 (dd, $J_{5,4}$ = 10.2 Hz, $J_{5,6}$ = 2.7 Hz, 1 H, H-5), 2.09, 2.07, 2.05, 2.03, 1.98 (5 s, each 3 H, 5 × CH_3).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.47, 170.08, 169.81, 169.77, 169.40, 169.23 (C=O), 133.78 (SPh, CH), 131.01 (SPh, Cq), 128.92 (SPh, CH), 128.66 (SPh, CH), 89.65 (C-1α), 85.55 (C-1β), 77.17 (C-5β), 74.11 (C-3β), 71.46 (C-5α), 70.54 (C-2α), 69.90 (C-6β), 69.78 (C-2β), 69.56 (C-3α), 69.36 (C-6α), 68.83 (C-4β), 68.39 (C-4α), 61.38 (C-7α, 7β), 20.84, 20.77, 20.72, 20.68, 20.66, 20.59, 20.58, 20.55 (CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{28}O_{11}SNa$: 535.1245; found: 535.1247.

Further elution of the column (toluene/EtOAc, 1:1) afforded 219 mg (39%) of **17** (α-anomer); R_f = 0.56 (EtOAc/hexane, 1:1).

2,3,4,6,7-Penta-*O*-acetyl-1,5-anhydro-D-*glycero*-D-*gluco*-heptitol (20)

Compound **19** (53 mg, 103 µmol) was dissolved in EtOH (50 mL) and dethionated in an H-Cube for 32 h (H-Cube SS; cartridge: Raney-Ni 33 mm; solvent: EtOH; flow rate: 0.2 mL; H_2-mode: full; temperature: 40 °C). The reaction mixture was concentrated and the residue was purified by column chromatography (toluene/acetone, 14:1) to give **20** (23 mg, 57 µmol, 55%) as a colorless oil; $[\alpha]_D^{20}$ +37.3 (*c* 1.2, $CHCl_3$). The reaction mixture was concentrated to dryness and directly purified by column chromatography (silica gel, toluene/acetone 14/1) to give the title compound (23 mg, 57 µmol, 55%) as colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 5.18–5.13 (m, 2 H, H-3, H-6), 5.04 (t, $J_{4,5}$ = $J_{3,4}$ = 9.9 Hz, 1 H, H-4), 4.95 (dt, $J_{2,1b}$ = 10.9 Hz, $J_{2,1b}$ = 5.5 Hz, $J_{2,3}$ = 9.9 Hz, 1 H, H-2), 4.31 (dd, $J_{7a,6}$ = 4.1 Hz, $J_{7a,7b}$ = 11.9 Hz, 1 H, H-7a), 4.17 (dd, $J_{7b,6}$ = 7.5 Hz, 1 H, H-7b), 4.14 (dd, $J_{1a,1b}$ = 11.2 Hz, $J_{2,1a}$ = 5.6 Hz, 1 H, H-1a), 3.62 (dd, $J_{5,4}$ = 10.1 Hz, $J_{5,6}$ = 2.5 Hz, 1 H, H-5), 3.26 (t, $J_{1a,1b}$ = 10.9 Hz, $J_{1b,2}$ = 10.9 Hz, 1 H, H-1b), 2.09, 2.07, 2.04, 2.02, 2.02 (5 s, each 3 H, 5 × CH_3).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.55, 170.24, 169.92, 169.75, 169.57 (5 × C=O), 77.96 (C-5), 73.68 (C-3), 69.95 (C-6), 69.03 (C-4), 68.74 (C-2), 66.77 (C-1), 61.41 (C-7), 20.90–20.65 (5 × CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{24}O_{11}Na$: 427.1211; found: 427.1214.

1,5-Anhydro-D-*glycero*-D-*gluco*-heptitol (21)

A solution of NaOMe in MeOH (100 µL, 0.1 M) was added to a solution of **20** (23.6 mg, 58 µmol) in MeOH (2 mL) at r.t. and the reaction mixture was stirred for 4 h. The mixture was then neutralized by addition of Dowex resin (50 H$^+$-form), filtered and the filtrate was concentrated. The residue was taken up in HPLC grade H_2O and purified over a short PD-10 column (Sephadex G-25, 1.45 × 5.0 cm, 8.3 mL column volume, eluent: H_2O). Product containing fractions were pooled and lyophilized to give **21** (10.5 mg, 92%) as an amorphous solid; $[\alpha]_D^{20}$ +28.2 (*c* 0.5, H_2O).

^{1}H NMR (600 MHz, D_2O): δ = 3.96 (dt, $J_{6,7a}$ = 3.4 Hz, $J_{6,7b}$ = 7.5 Hz, 1 H, H-6), 3.92 (dd, $J_{1a,1b}$ = 11.0 Hz, $J_{1a,2}$ = 5.4 Hz, 1 H, H-1a), 3.72 (dd, $J_{7a,7b}$ = 12.0 Hz, 1 H, H-7a), 3.63 (dd, $J_{7a,7b}$ = 12.0 Hz, $J_{7a,6}$ = 7.6 Hz, 1 H, H-7b), 3.53 (ddd, $J_{2,3}$ ≅ 10.5 Hz, 1 H, H-2), 3.43 (t, $J_{4,3}$ = $J_{4,5}$ = 9.3 Hz, 1 H, H-4), 3.39–3.35 (m, 2 H, H-3, H-5), 3.19 (t, $J_{1b,2}$ = 10.9 Hz, 1 H, H-1b).

^{13}C NMR (150 MHz, D_2O): δ = 80.62 (C-5), 77.56 (C-3), 71.59 (C-6), 70.13 (C-4), 69.05 (C-2), 68.91 (C-1), 61.43 (C-7).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_7H_{14}O_6Na$: 217.0683; found: 217.0682.

3,4,6,7-Tetra-*O*-acetyl-1,5-anhydro-2-deoxy-D-*altro*-hept-1-enitol (22)

Compound **17** (500 mg, 0.43 mmol) was dissolved in HBr (33% in AcOH, 2.5 mL) and stirred at r.t. for 12 h. When according to TLC all starting materials had been converted to a higher running spot, NaOAc (2.3 g, 28 mmol) was slowly added at 0 °C. The mixture was diluted with AcOH (3 mL) and placed in an ice-cold ultrasonic bath. Zn dust (500 mg, 7.7 mmol) was added slowly and the mixture was allowed to react under sonication at 0 °C for 30 min (toluene/EtOAc, 3:1). The mixture was diluted with AcOH (5 mL) and CH_2Cl_2 (20 mL) and the Zn dust was filtered off. The filter was washed with CH_2Cl_2 and the filtrate was diluted with CH_2Cl_2 (20 mL) and washed with H_2O. The organic phase was concentrated and solid $NaHCO_3$ was added. The residue was dissolved in CH_2Cl_2, washed with H_2O, dried ($MgSO_4$), and concentrated. Flash chromatography through a short plug of silica gel (2 g, Isolute Si II, toluene/EtOAc, 1:1) followed by HPLC (column: YMC Pack SIL 06, 20 × 250, toluene/EtOAc, 8:1, flow rate 5 mL/m, fraction size 5 mL) gave **22** (290 mg, 75%) as a colorless oil; $[\alpha]_D^{20}$ –35.5 (*c* 2.1, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.48 (dd, $J_{1,2}$ = 6.2 Hz, $J_{1,3}$ = 0.8 Hz, 1 H, H-1), 5.37 (ddd, $J_{6,5}$ = 8.1 Hz, $J_{6,7a}$ = 3.0 Hz, $J_{6,7b}$ = 4.9 Hz, 1 H, H-6), 5.22 (ddd, $J_{4,5}$ = 4.3 Hz, $J_{4,3}$ = 3.5 Hz, 1 H, H-4), 5.07 (ddt, $J_{3,2}$ = 4.4 Hz, 1 H, H-3), 4.97 (ddd, $J_{2,1}$ = 6.2 Hz, $J_{2,3}$ = 4.4 Hz, $J_{2,4}$ = 1.1 Hz, 1 H, H-2), 4.48 (dd, $J_{7a,7b}$ = 12.3 Hz, $J_{7a,6}$ = 2.9 Hz, 1 H, H-7a), 4.36 (ddd, $J_{5,4}$ = 8.3 Hz, $J_{5,6}$ = 4.4 Hz, $J_{5,3}$ = 1.4 Hz, 1 H, H-5), 4.13 (dd, $J_{7b,6}$ = 4.8 Hz, $J_{7a,7b}$ = 12.3 Hz, 1 H, H-7b), 2.10, 2.08, 2.06, 1.98 (4 s, each 3 H, 4 × CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.55, 169.95, 169.48, 169.43 (q, 4 × C=O), 145.28 (C-1), 98.53 (C-2), 72.45 (C-5), 67.62 (C-6), 66.74 (C-4), 64.56 (C-3), 61.75 (C-7), 20.86, 20.85, 20.78, 20.68 (4 × CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{20}O_9Na$: 367.1000; found: 367.0997.

1,5-Anhydro-2-deoxy-D-*altro*-hept-1-enitol (23)

A 0.1 M solution of methanolic NaOMe (58 µL) was added to a cooled (0 °C) solution of **22** (20 mg, 58 µmol) in MeOH (1 mL) and stirred at 0 °C for 3 h. The reaction mixture was neutralized (Dowex H$^+$), filtered, and flashed through a short plug of reversed phase (RP) silica gel (500 mg, eluent: H_2O). The product containing fractions were lyophilized to give the target compound **23** (9.2 mg, 90%) as a colorless amorphous solid; $[\alpha]_D^{21}$ –14 (*c* 0.9, H_2O).

^{1}H NMR (600 MHz, D_2O): δ = 6.40 (dd, $J_{1,2}$ = 6.0 Hz, $J_{1,3}$ = 1.5 Hz, 1 H, H-1), 4.81 (dd, $J_{2,1}$ = 6.0 Hz, $J_{2,3}$ = 2.7 Hz, 1 H, H-2), 4.20–4.18 (m, 1 H, H-3), 4.11 (quin, *J* = 3.7 Hz, $J_{7,6b}$ = 7.5 Hz, H-6), 3.94 (dd, $J_{5,4}$ = 8.8 Hz, $J_{5,6}$ = 4.3 Hz, 1 H, H-5), 3.79–3.75 (m, 2 H, H-7a, H-4), 3.69 (dd, $J_{7b,7a}$ = 12.0 Hz, $J_{7b,6}$ = 7.2 Hz, 1 H, H-7b).

^{13}C NMR (150 MHz, D_2O): δ = 144.72 (C-1), 103.35 (C-2), 78.89 (C-5), 71.34 (C-6), 69.94 (C-4), 68.85 (C-3), 62.55 (C-7).

HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_7H_{12}O_5$: 175.0612; found: 175.0615.

3,4,6,7-Tetra-*O*-acetyl-1,5-anhydro-1,2-dideoxy-D-*altro*-heptitol (24)

Pd/C (10%, 2 mg) was added to a solution of compound **22** (21 mg, 61 mmol) in THF (1 mL) and stirred under H_2 atmosphere (1 bar) for 12 h at r.t. The reaction mixture was filtered through a syringe filter and the syringe filter was washed with THF (5 mL). The filtrates were combined and concentrated, flashed through a short plug of silica gel (2 g Isolute SI II), and purified via HPLC (hexane/EtOAc, 2:1) to give **24** (18 mg, 85%) as a colorless oil; $[\alpha]_D^{20}$ +29.8 (*c* 1.8, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 5.17 (ddd, $J_{6,7b}$ = 7.8 Hz, $J_{6,7a}$ = 3.7 Hz, $J_{6,5}$ = 2.4 Hz, H-6), 4.95–4.90 (m, 2 H, H-3, H-4), 4.34 (dd, $J_{7a,7b}$ = 12.0 Hz, $J_{7a,6}$ = 3.7 Hz, 1 H, H-7a), 4.20 (dd, $J_{7a,7b}$ = 12.0 Hz, $J_{7b,6}$ = 7.8 Hz, 1 H, H-7b), 4.01 (ddd, $J_{1a,1b}$ = 12.0 Hz, $J_{1a,2a}$ = 4.9 Hz, $J_{1a,2b}$ = 1.9 Hz, 1 H, H-1a), 3.56–3.51 (m, 1 H, H-5), 3.45 (td, *J* = 12.2, 12.2, 2.3 Hz, 1 H, H-1b), 2.09–2.05 (m, 1 H, H-2a), 2.09, 2.08, 2.03, 2.02 (4 s, each 3 H, 4 × CH_3), 1.79–1.71 (m, 1 H, H-2b).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.61, 170.30, 170.02, 169.87 (q, 4 × C=O), 78.10 (C-5), 72.23 (C-4), 70.20 (C-6), 69.64 (C-3), 65.21 (C-1), 61.72 (C-7), 30.70 (C-2), 20.91, 20.73, 20.70 (4 × CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{22}O_9Na$: 369.1156; found: 369.1155.

1,5-Anhydro-1,2-dideoxy-D-*altro*-heptitol (25)

A solution of methanolic 0.1 M NaOMe (52 µL) was added to a cooled (0 °C) solution of **24** (18 mg, 52 µmol) in MeOH (1 mL) and stirred at 0 °C for 3 h. The reaction mixture was neutralized (Dowex H$^+$), filtered, and flashed through a short plug of RP silica gel (500 mg, eluent: H_2O). Product containing fractions were lyophilized to give **25** (9.0 mg, 98%) as a colorless amorphous solid; $[\alpha]_D^{20}$ +9.5 (*c* 0.9, H_2O).

^{1}H NMR (600 MHz, D_2O): δ = 3.98 (dt, *J* = 3.0, 3.0 Hz, $J_{6,7b}$ = 7.5 Hz, 1 H, H-6), 3.93 (ddd, $J_{1a,1b}$ = 11.8 Hz, $J_{1a,2a}$ = 5.0 Hz, $J_{1a,2b}$ = 1.6 Hz, 1 H, H-1a), 3.74 (dd, $J_{7a,7b}$ = 11.9 Hz, $J_{7a,6}$ = 3.4 Hz, 1 H, H-7a), 3.65 (dd, $J_{7b,6}$ = 7.5 Hz, $J_{7a,7b}$ = 11.9 Hz, 1 H, H-7b), 3.61 (ddd, $J_{3,2b}$ = 11.4 Hz, $J_{3,4}$ = 8.2 Hz, $J_{3,2a}$ = 5.0 Hz, 1 H, H-3), 3.45 (td, $J_{1b,1a}$ = $J_{1b,2b}$ = 12.2 Hz, $J_{1b,2a}$ = 1.9 Hz, 1 H, H-1b), 3.34 (dd, $J_{4,3}$ = 8.2 Hz, $J_{4,5}$ = 9.8 Hz, 1 H, H-4), 3.31 (dd, $J_{5,6}$ = 2.8 Hz, $J_{5,4}$ = 9.8 Hz, 1 H, H-5), 1.95 (ddt, $J_{2a,2b}$ = 13.1 Hz, $J_{2a,3}$ = 5.1 Hz, $J_{2a,1b}$ = 1.8 Hz, 1 H, H-2a), 1.61–1.54 (ddd, *J* = 5.0 Hz, *J* = 11.6 Hz, *J* = 12.8 Hz, 1 H, H-2b).

^{13}C NMR (150 MHz, D_2O): δ = 81.64 (C-5), 73.21 (C-3), 72.85 (C-4), 72.69 (C-6), 66.57 (C-1), 62.61 (C-7), 33.66 (C-2).

HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_7H_{14}O_5$: 177.0768; found: 177.0767.

7-*O*-Triisopropylsilyl-1,5-anhydro-D-*glycero*-D-*gluco*-heptitol (26)

TIPSCl (39 µL, 0.184 mmol) was added dropwise to a solution of **21** (34 mg, 0.175 mmol) and imidazole (36 mg, 0.526 mmol) in freshly distilled THF (5 mL) at 0 °C under argon. After 2 h, additional TIPSCl (13 µL) was added and the reaction mixture was stirred for further 12 h. Additional reagents were added portionwise every 60 min (in total 60 µL TIPSCl and 24 mg imidazole) and the mixture was stirred for further 12 h, when TLC showed complete consumption of the starting material. The mixture was concentrated, and partitioned between CH_2Cl_2 (10 mL) and sat. aq NH_4Cl (6 mL). The aqueous phase was reextracted with CH_2Cl_2 (2 × 5 mL) and the combined organic phase was washed with brine (10 mL), dried ($MgSO_4$), and concentrated. Purification of the residue on silica gel (EtOAc/toluene, 3:1) and HPLC ($CHCl_3$/EtOH, 25:1) gave **26** as a colorless oil (20 mg, 32%); $[\alpha]_D^{20}$ +7.7 (*c* 1.0, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 4.49 (d, $J_{4,OH}$ = 1.0 Hz, 1 H, OH-4), 4.14 (br s, 1 H, OH-3), 3.93 (dd, $J_{1e,1a}$ = 11.1 Hz, $J_{1e,2}$ = 5.4 Hz, 1 H, H-1e), 3.86 (dd, $J_{7a,7b}$ = 12.1 Hz, $J_{6,7a}$ = 3.4 Hz, 1 H, H-7a), 3.81–3.75 (m, 2 H, H-6, H-7b), 3.65 (dddd, $J_{2,1a}$ = 10.4 Hz, $J_{2,3}$ = 9.0 Hz, 1 H, H-2), 3.58 (br t, $J_{4,3}$ = 9.0 Hz, 1 H, H-4), 3.53 (d, *J* = 2.6 Hz, 1 H, OH-2), 3.50 (br t, *J* = 8.9 Hz, 1 H, H-3), 3.19 (dd, $J_{5,6}$ = 5.2 Hz, $J_{5,4}$ = 8.5 Hz, 1 H, H-5), 3.17 (m, 2 H, H-1a, OH-6), 1.17–1.09 [m, 3 H, 3 × SiC*H*$(CH_3)_2$], 1.08–1.05 [m, 18 H, 3 × SiCH$(CH_3)_2$].

^{13}C NMR (150 MHz, $CDCl_3$): δ = 78.55 (C-3), 77.26 (C-5), 74.68 (C-6), 73.95 (C-4), 69.49 (C-2), 69.16 (C-1), 63.77 (C-7), 17.88, 17.88, 17.86 [SiCH$(CH_3)_2$], 11.85 [Si(*C*H$(CH_3)_2$].

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{34}O_6SiNa$: 373.2017; found: 373.2015.

2,3,4,6-Tetra-*O*-benzyl-7-*O*-triisopropylsilyl-1,5-anhydro-D-*glycero*-D-*gluco*-heptitol (27)

NaH (60% in mineral oil, 18 mg, 0.457 mmol) was added to a stirred solution of **26** (20 mg, 57 µmol) in anhyd DMF (3 mL) under argon. After 20 min, BnBr (33 µL, 0.274 mmol) was added at 0 °C and the mixture was stirred at r.t. for 15 h. Additional BnBr (0.8 equiv, 5.5 µL) was then added at 0 °C and stirring was continued for 1.5 h. MeOH (20 µL) was added dropwise at 0 °C and the mixture was warmed to r.t. The solution was diluted with Et_2O (10 mL), and washed with H_2O (5 mL) and sat aq $NaHCO_3$ (5 mL). The aqueous layers were extracted once more with Et_2O (10 mL), the combined organic layers were dried ($MgSO_4$), filtered, and the solvent was removed under vacuum. The residual oil was purified by HPLC (hexane/EtOAc, 20:1) to give **27** as a colorless oil (22 mg, 54%); $[\alpha]_D^{20}$ +3.2 (*c* 1.1, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.36–7.14 (m, 20 H, 4 × ArH), 4.97–4.61 (m, 8 H, 4 × OCH_2Ph), 4.02 (dd, $J_{1e,1a}$ = 11.2 Hz, $J_{1e,2}$ = 5.0 Hz, 1 H, H-1e), 3.89 (dd, $J_{7a,7b}$ = 8.8 Hz, $J_{7a,6}$ = 4.0 Hz, 1-H, H-7a), 3.87–3.80 (m, 2 H, H-7b, H-6), 3.66 (app t, *J* = 8.8 Hz, 1 H, H-4), 3.62 (t, $J_{3,4}$ = $J_{3,2}$ = 8.6 Hz, 1 H, H-3), 3.58 (ddd, $J_{2,3}$ = 8.6 Hz, $J_{2,1e}$ = 5.2 Hz, 1 H, H-2), 3.49 (br d, $J_{5,4}$ = 9.6 Hz, 1 H, H-5), 3.17 (app t, *J* = 10.6 Hz, 1 H, H-1a), 1.07–0.97 [m, 21 H, 3 × SiC*H*$(CH_3)_2$].

^{13}C NMR (150 MHz, $CDCl_3$): δ = 138.81, 138.77, 138.36 (q, ArC), 128.46, 128.38, 128.29, 128.22, 127.84, 127.81, 127.78, 127.70, 127.66, 127.56, 127.43, 127.35 (ArC), 86.81 (C-3), 80.71 (C-6), 80.57 (C-5), 78.66 (C-2), 78.30 (C-4), 75.56, 74.79, 73.22, 72.99 (4 × O*C*H_2Ph), 68.17 (C-1), 63.95 (C-7), 18.01 [Si(CH(*C*$H_3)_2$], 11.88 [Si(*C*H$(CH_3)_2$].

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{44}H_{58}O_6SiNa$: 733.3895; found: 733.3894.

2,3,4,6-Tetra-*O*-benzyl-1,5-anhydro-D-*glycero*-D-*gluco*-heptitol (28)

Compound **27** (22 mg, 31 µmol) was dissolved in anhyd THF (3 mL), TBAF (124 µL of a 1 M solution in THF) was added and the reaction mixture was stirred at r.t. for 17 h. The solution was diluted with Et_2O (10 mL) and successively washed with sat. aq NH_4Cl (5 mL) and H_2O (5 mL). The aqueous layers were reextracted with Et_2O (10 mL), the combined organics were dried ($MgSO_4$), concentrated, and the remaining oil was directly purified by HPLC (toluene/EtOAc, 6:1) to give **28** (14 mg, 82%) as a colorless oil; $[\alpha]_D^{20}$ +18.1 (*c* 0.7, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.34–7.14 (m, 20 H, 4 × ArH), 4.90, 4.74, 4.66, 4.63 (8 H, 4 × OCH_2Ph), 4.02 (dd, $J_{1e,1a}$ = 11.3 Hz, $J_{1e,2}$ = 5.2 Hz, 1 H, H-1e), 3.72 (ddd, $J_{6,5}$ = 1.2 Hz, $J_{6,7b}$ = 4.2 Hz, $J_{6,7a}$ = 6.4 Hz, 1 H, H-6), 3.67 (ddd, $J_{7a,7b}$ = 11.9 Hz, $J_{7a,OH}$ = 2.3 Hz, 1 H, H-7a), 3.64 (dd, $J_{3,4}$ = 8.3 Hz, $J_{3,2}$ = 9.0 Hz, 1 H, H-3), 3.59 (ddd, $J_{2,1a}$ = 10.3 Hz, $J_{2,1e}$ = 5.2 Hz, $J_{2,3}$ = 8.3 Hz, 1 H, H-2), 3.59–3.55 (m, 1 H, H-7b), 3.51 (dd, $J_{5,4}$ = 10.0 Hz, $J_{6,5}$ = 1.2 Hz, 1 H, H-5), 3.46 (dd, $J_{4,5}$ = 10.0 Hz, $J_{4,3}$ = 8.3 Hz, 1 H, H-4), 3.15 (dd, $J_{1a,2}$ = 10.4 Hz, 1 H, H-1a), 2.04 (dd, *J* = 9.0 Hz, *J* = 2.3 Hz, 1 H, CH_2OH).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 138.52, 138.15, 138.11, 137.78 (q, 4 × ArC), 128.59–127.69 (ArCH), 86.72 (C-3), 80.81 (C-5), 78.61 (C-2), 78.51 (C-6), 77.51 (C-4), 75.65, 74.86, 73.26, 71.97 (4 × OCH_2Ph), 68.25 (C-1), 61.41 (C-7).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{35}H_{38}O_6Na$: 577.2561; found: 577.2559.

2,3,4,6-Tetra-*O*-benzyl-7-*O*-[bis(benzyloxy)phosphoryl]-1,5-anhydro-D-*glycero*-D-*gluco*-heptitol (29)

Compound **28** (14 mg, 25 µmol) was twice co-evaporated with toluene and dried under vacuum for 12 h. The material was dissolved in anhyd CH_2Cl_2 (3 mL), dibenzyl-*N*,*N*-diisopropylaminophosphoramidite reagent (8 µL, 25 µmol) was added, and the mixture was stirred at r.t. for 20 min. 1*H*-Tetrazole (0.45 M in MeCN, 56 µL, 25 µmol) was added slowly and the solution was stirred at r.t. for 20 min. Additional reagent was added portionwise every 20 min until the starting material was consumed (in total 12 µL = 36 mmol amidite reagent and 79 µL of tetrazole solution were used). The solution was cooled to –78 °C and a solution of *m*CPBA (70%, 16 mg, 63 µmol) in CH_2Cl_2 (1 mL) was added slowly to the reaction mixture. After 60 min, Et_3N (8.8 µL, 63 mmol) was added and the mixture was allowed to warm up to r.t. The solution was diluted with CH_2Cl_2 (10 mL), washed with sat. aq $NaHCO_3$ (2 × 5 mL), dried ($MgSO_4$), and concentrated. The residue was purified by HPLC (toluene/EtOAc, 8:1, containing 0.5% Et_3N) to give **29** as a colorless oil (18 mg, 22 mmol, 85%); $[\alpha]_D^{20}$ +4.2 (*c* 0.9, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.34–7.12 (m, 30 H, ArH), 5.03–4.56 (m, 12 H, 6 × OCH_2Ph), 4.15 (dd, $J_{7,P}$ = 6.8 Hz, $J_{7a\text{ or }7b/6}$ = 5.8 Hz, 2 H, H-7a, H-7b), 3.97 (dd, $J_{1e,1a}$ = 11.3 Hz, $J_{1e,2}$ = 5.2 Hz, 1 H, H-1e), 3.92 (dt, $J_{6/7a\text{ or }7b}$ = 5.8 Hz, 1 H, H-6), 3.59 (t, $J_{3,4}$ = $J_{3,2}$ = 8.7 Hz, 1 H, H-3), 3.54 (dd, $J_{2,1a}$ = 10.5 Hz, 1 H, H-2), 3.49 (dd, $J_{4,5}$ = 9.8 Hz, 1 H, H-4), 3.42 (br d, $J_{4,5}$ = 10.0 Hz, 1 H, H-5), 3.13 (t, *J*= 11.0 Hz, Hz, 1 H, H-1a).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 128.58–128.22 and 127.96–127.57 (ArC), 86.59 (C-3), 80.02 (C-5), 75.51 (C-2), 78.26 ($J_{P,6}$ = 7.3 Hz, C-6), 77.68 (C-4), 75.54, 74.83, 73.23, 72.84 (4 × OCH_2Ph), 69.33–69.18 (POCH_2Ph), 68.10 (C-1), 67.49 ($J_{P,7}$ = 5.8 Hz, C-7).

^{31}P NMR (242.94 MHz, $CDCl_3$): δ = –0.93.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{49}H_{51}O_9P$: 815.3343; found: 815.3345.

1,5-Anhydro-D-*glycero*-D-*gluco*-heptitol-7-phosphate Triethylammonium Salt (30)

A suspension of **29** (18 mg, 0.022 mmol), and 10% Pd/C (2 mg) in 5:3:2 EtOH/EtOAc/H_2O (3 mL) was stirred under H_2 atmosphere (1 bar) at r.t. for 48 h. Fresh catalyst (2 mg) was added after 16 h and 32 h. The reaction mixture was then filtered through a short plug of Celite and the Celite bed was successively washed with H_2O (20 mL). The filtrate was passed through a short gel column (PD-10 prepacked, 8.3 mL G-25, H_2O). Et_3N (6 µL) was added and the solution was concentrated. The residue was dissolved in H_2O (3 mL), aliquoted into three batches of 1 mL, filtered through a syringe filter, and lyophilized to give three batches of compound **30** (1.9, 2.8, and 2.1 mg, respectively, in total 6.8 mg, 99%) as a colorless amorphous solid; $[\alpha]_D^{20}$ +35.2 (*c* 0.4, H_2O).

^{1}H NMR (600 MHz, D_2O): δ = 4.12 (dt, $J_{6,7a}$ = 3.8 Hz, $J_{6,7b}$ = 7.3 Hz, 1 H, H-6), 3.95 (dd, $J_{1e,1a}$ = 11.0 Hz, $J_{1e,2}$ = 5.3 Hz, 1 H, H-1e), 3.94 (br d, $J_{7a,7b}$ = 11.9 Hz, $J_{7a,6}$ = 3.8 Hz, 1 H, H-7a), 3.82 (dd, $J_{7b,7a}$ = 11.4 Hz, $J_{7b,P}$ = 7.3 Hz, 1 H, H-7b), 3.58 (ddd, $J_{2,3}$ = 9.1 Hz, $J_{1e,2}$ = 5.5 Hz, 1 H, H-2), 3.53 (br t, $J_{4,3}$ = 9.4 Hz, $J_{4,5}$ = 9.8 Hz, 1 H, H-4), 3.41 (dd, $J_{5,6}$ = 2.5 Hz, $J_{5,4}$ = 9.8

Hz, 1 H, H-5), 3.39 (br t, $J_{2,3} = J_{3,4}$ = 9.1 Hz, 1 H, H-3), 3.22 (t, $J_{1a,2}$ = 10.3 Hz, $J_{1a,1e}$ = 11.0 Hz, 1 H, H-1a), 3.18 (q, J= 7.3 Hz, 2.6 H, NCH_2), 1.26 (t, J= 7.3 Hz, 4 H, NCH_2CH_3).

^{13}C NMR (150 MHz, D_2O): δ = 81.52 (C-5), 78.25 (C-3), 71.59 ($J_{6,P}$ = 6.0 Hz, C-6), 70.58 (C-4), 69.91 (C-2), 69.74 (C-1), 64.84 ($J_{7,P}$ = 4.4 Hz, C-7), 47.29 (NCH_2), 8.85 (NCH_2CH_3).

^{31}P NMR (242 MHz, D_2O): δ = 3.95.

HRMS (ESI): m/z [M + H]$^+$ calcd for $C_7H_{15}O_9P$: 275.0526; found: 275.0525.

3-*O*-Benzyl-1,2-*O*-isopropylidene-7-*O*-triisopropylsilyl-D-*glycero*-α-D-*gluco*-heptofuranose (31)

TIPSCl (165 µL, 772 µmol) was added dropwise to a solution of triol **14** (250 mg, 735 µmol) and DABCO (247 mg, 2.2 mmol) in freshly distilled THF (10 mL) at 0 °C under argon. The following reagents were added until the starting material was completely consumed: TIPSCl (165 µL, 0.772 mmol) and DABCO (247 mg, 726 µmol) after 18 h, and TIPSCl (41 µL, 192 mmol) and DABCO (62 mg, 18 µmol) after 42 h. The reaction mixture was concentrated to dryness, taken up in CH_2Cl_2 (10 mL) and sat. aq NH_4Cl (6 mL) was added. The aqueous phase was reextracted with CH_2Cl_2 (2 × 5 mL) and the combined organic phases were washed with brine (10 mL), dried ($MgSO_4$), and concentrated. The residue was purified on silica gel (toluene/EtOAc, 10:1) to give **31** as a colorless oil (260 mg, 71%); $[\alpha]_D^{20}$ –26.4 (c 1.1, $CDCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.37–7.28 (m, 5 H, C_6H_5), 5.95 (d, $J_{1,2}$ = 3.7 Hz, 1 H, H-1), 4.69 (d, J = 11.5 Hz, 1 H, OCH_2Ph), 4.63 (d, J = 11.5 Hz, 1 H, OCH_2Ph), 4.59 (d, $J_{2,1}$ = 3.7 Hz, 1 H, H-2), 4.26 (dd, $J_{4,3}$ = 3.0 Hz, $J_{4,5}$ = 7.5 Hz, 1 H, H-4), 4.20 (d, $J_{3,4} \cong$ 3.0 Hz, 1 H, H-3), 4.11 (q, $J_{5,4} = J_{5,6}$ = 7.0 Hz, 1 H, H-5), 4.00 (dd, $J_{7a,7b}$ = 10.2 Hz, $J_{7a,6}$ = 4.9 Hz, 1 H, H-7a), 3.93 (dd, $J_{7b,6}$ = 4.0 Hz, 1 H, H-7b), 3.75–3.70 (m, 1 H, H-6), 3.49 (d, J = 7.1 Hz, 1 H, 5-OH), 2.98 (d, J = 5.4 Hz, 1 H, 6-OH), 1.48 (s, 3 H, CH_3), 1.32 (s, 3 H, CH_3), 1.17–1.10 [m, 3 H, 3 × $SiCH(CH_3)_3$], 1.09–1.05 [m, 18 H, 3 × $SiCH(CH_3)_2$].

^{13}C NMR (150 MHz, $CDCl_3$): δ = 137.22 (q, ArC), 128.54, 128.06, 127.83 (ArC), 111.77 [$C(CH_3)_2$], 105.11 (C-1), 82.56 (C-3), 82.10 (C-2), 80.46 (C-4), 72.51 (OCH_2Ph), 71.80 (C-6), 70.63 (C-5), 65.47 (C-7), 26.77, 26.26 [$CH(CH_3)_2$], 17.91 [$SiCH(CH_3)_2$], 11.78 [$SiCH(CH_3)_2$].

HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{26}H_{44}O_7Si$: 497.2929; found: 497.2923.

3,5,6-Tri-*O*-benzyl-1,2-*O*-isopropylidene-7-*O*-triisopropylsilyl-D-*glycero*-α-D-glucofuranose (32)

Triflic acid (0.25 µL, 2.8 µmol) was added to a solution of diol **31** (26 mg, 60 µmol) and benzyl 2,2,2-trichloroacetimidate (39 µL, 242 µmol) in anhyd CH_2Cl_2 (3 mL) at 0 °C under argon. After 2 h, additional benzyl 2,2,2-trichloroacetimidate (20 µL, 124 µmol) was added and the mixture stirred for 30 min. Sat. aq $NaHCO_3$ (2 mL) was added, the phases were separated and the aqueous phase was reextracted with CH_2Cl_2 (2 mL). The combined organic phases were dried ($MgSO_4$), concentrated, and the residue was purified by chromatography (silica gel 60, hexane/EtOAc, 15:1) to give **32** (30 mg, 85%) as a syrup.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.45–7.18 (m, 15 H, 3 × ArH), 5.89 (d, $J_{1,2}$ = 3.7 Hz, 1 H, H-1), 4.87–4.57 (m, 4 H, 2 × OCH_2Ph), 4.55 (d, $J_{2,1}$ = 3.7 Hz, 1 H, H-2), 4.48–4.39 (m, 2 H, OCH_2Ph), 4.32 (dd, $J_{4,3}$ = 3.0 Hz, $J_{4,5}$ = 9.5 Hz, 1 H, H-4), 4.17 (dd, $J_{5,6}$ = 0.8 Hz, 1 H, H-5), 4.08 (d, J = 3.0 Hz, 1 H, H-3), 4.04–3.93 (m, 3 H, H-6, H-7a, H-7b), 1.44 and 1.29 [$C(CH_3)_2$], 1.13–1.00 [m, 21 H, 3 × $Si(CH(CH_3)_2$].

^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.39, 138.83, 137.70 (q, ArC), 128.51, 128.37, 128.26, 128.20, 128.09, 127.70, 127.69, 127.49, 127.41, 127.35, 127.08 (ArC), 111.65 [$C(CH_3)_2$], 105.24 (C-1), 82.24 (C-3), 81.76 (C-6), 81.50 (C-2), 79.06 (C-4), 76.89 (C-5), 73.22, 73.13, 71.91 (3 × OCH_2Ph), 63.61 (C-7), 26.78, 26.38 [$C(CH_3)_2$], 18.04 [$Si(CH(CH_3)_2$], 11.92 [$Si(CH(CH_3)_2$].

LC-MS: m/z [M + NH_4]$^+$ calcd for $C_{40}H_{60}NO_7Si$: 694.4; found: 694.8.

3,5,6-Tri-*O*-benzyl-1,2-*O*-isopropylidene-D-*glycero*-α-D-*gluco*-heptofuranose (33)

A 1 M solution of TBAF in THF (126 µL) was added to a solution of **32** (30 mg, 42 µmol) in anhyd THF (3 mL) and the mixture was stirred at r.t. for 5 h. The solution was diluted with Et_2O (10 mL) and successively washed with sat. aq NH_4Cl (5 mL) and H_2O (5 mL). The aqueous layers were extracted once more with Et_2O (10 mL), the combined organic phases were dried ($MgSO_4$), concentrated, and the residual oil was purified by chromatography (hexane/EtOAc, 3:1) to give **33** as a colorless oil (14 mg, 60%); $[\alpha]_D^{20}$ –30 (c 1.2, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.37–7.20 (m, 15 H, ArH), 5.90 (d, $J_{1,2}$ = 3.7 Hz, 1 H, H-1), 4.88 (d, J = 11.1 Hz, 1 H, OCH_2Ph), 4.67 (d, J = 11.7 Hz, 1 H, OCH_2Ph), 4.66 (d, J = 11.7 Hz, 1 H, OCH_2Ph), 4.62 (d, J = 11.5 Hz, 1 H, OCH_2Ph), 4.58 (d, $J_{2,1}$ = 3.7 Hz, 1 H, H-2), 4.45 (d, J = 11.5 Hz, 2 H, OCH_2Ph), 4.28 (dd, $J_{4,3}$ = 3.0 Hz, $J_{4,5} \cong$ 9.0 Hz, 1 H, H-4), 4.22 (dd, $J_{4,5} \cong$ 9.0 Hz, $J_{5,6}$ = 1.4 Hz, 1 H, H-5), 4.10 (d, $J_{3,4}$ = 3.0 Hz, 1 H, H-3), 3.95–3.85 (m, 3 H, H-6, H-7a, H-7b), 2.43 (dd, J = 2.8 Hz, J = 8.6 Hz, 1 H, 7-OH), 1.47 [s, 3 H, $C(CH_3)_2$], 1.30 [s, 3 H, $C(CH_3)_2$].

^{13}C NMR (150 MHz, $CDCl_3$): δ = 138.53, 138.41, 137.38 (q, ArC), 128.52, 128.46, 128.40, 128.35, 127.98, 127.70, 127.69, 127.60, 127.45 (ArCH), 111.96 [$C(CH_3)_2$], 105.16 (C-1), 81.99 (C-3), 81.44 (C-2), 79.99 (C-6), 78.91 (C-4), 76.92 (C-5), 74.07, 71.99, 71.99 (3 × OCH_2Ph), 61.35 (C-7), 26.87 and 26.36 [$C(CH_3)_2$].

HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{31}H_{36}O_7Na$: 543.2353; found: 543.2357.

3,5,6-Tri-*O*-benzyl-7-*O*-[bis(benzyloxy)phosphoryl]-1,2-*O*-isopropylidene-D-*glycero*-α-D-*gluco*-heptofuranose (34)

Alcohol **33** (12 mg, 23 µmol) was twice co-evaporated with toluene, dried in vacuo for 12 h, and taken up in anhyd CH_2Cl_2 (3 mL). Dibenzyl-*N*,*N*-diisopropylaminophosphoramidite (8 µL, 25 µmol) was added and the mixture was stirred at r.t. for 20 min. 1*H*-Tetrazole [(0.3 M in MeCN (3 wt%), 75 µL, 25 µmol] was added very slowly and the solution was stirred at r.t. Additional reagent was added portionwise (0.4 equiv each) until the starting material was consumed (22 µL, 69 µmol of phosphoramidite and 230 µL of tetrazole, 69 µmol). The reaction mixture was stirred for further 30 min, cooled to –78 °C, and a solution of *m*CPBA (70%, 26 mg, 105 µmol) in CH_2Cl_2 (1 mL) was added slowly. The reaction mixture was stirred for 30 min. Et_3N (9.7 µL, 70 µmol) was added slowly and the mixture was warmed to r.t. The mixture was diluted with CH_2Cl_2 (10 mL), washed with sat. aq $NaHCO_3$ (2 × 5 mL), dried ($MgSO_4$), and concentrated. The residue was purified by chromatography (toluene/EtOAc, 6:1 containing 0.5% Et_3N) to give **34** as a colorless oil (14 mg, 18 µmol, 78%); $[\alpha]_D^{21}$ –22.4 (c 1.4, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.32–7.15 (m, 25 H, ArH), 5.87 (d, $J_{1,2}$ = 3.7 Hz, 1 H, H-1), 5.03–4.96 [m, 4 H, $P(OCH_2Ph)_2$], 4.75 (d, J = 11.4 Hz, 1 H, OCH_2Ph), 4.66 (s, 2 H, OCH_2Ph), 4.59 (d, J = 11.5 Hz, 1 H, OCH_2Ph), 4.55 (d, $J_{2,1}$ = 3.7 Hz, 1 H, H-2), 4.42 (d, J = 11.5 Hz, 1 H, OCH_2Ph), 4.39 (d, J = 11.4 Hz, 1 H, OCH_2Ph), 4.37–4.30 (m, 2 H, H-7a, H-7b), 4.29 (dd, $J_{4,3}$ = 3.1 Hz, $J_{4,5}$ = 9.4 Hz, 1 H, H-4), 4.11 (dd, $J_{5,4}$ = 9.4 Hz, $J_{5,6}$ = 1.2 Hz, 1 H, H-5), 4.09 (ddd, $J_{6,5}$ = 1.3 Hz, $J_{6,7}$ = 4.4, 6.6 Hz, 1 H, H-6), 4.06 (br d, $J_{3,4}$ = 3.1 Hz, 1 H, H-3), 1.43 [s, 3 H, $C(CH_3)_2$], 1.28 [s, 3 H, $C(CH_3)_2$].

^{13}C NMR (150 MHz, $CDCl_3$): δ = 138.54, 138.44, 137.43 (q, ArC), 136.00, 135.96 (q, $POCH_2ArC$), 128.46, 128.45, 128.32, 128.29, 128.25, 128.19, 127.88, 127.87, 127.79, 127.60, 127.51, 127.44, 127.37, 127.30 (ArCH), 111.86 [$C(CH_3)_2$], 105.19 (C-1), 82.06 (C-3), 81.50 (C-2), 79.28 (d, $J_{P,C}$ = 7.7 Hz, C-6), 78.72 (C-4), 76.50 (C-5), 73.43, 72.86, 72.00 (3 × OCH_2Ph), 69.12, 69.10 (2 d, $J_{P,C}$ = 5.3 Hz, $POCH_2Ph$), 67.46 (d, $J_{P,C}$ = 5.7 Hz, C-7), 26.83 and 26.37 [$C(CH_3)_2$].

^{31}P NMR (242.94 MHz, $CDCl_3$): δ = –0.98.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{45}H_{49}O_{10}PNa$: 803.2956; found: 803.2959.

D-*Glycero*-D-*gluco*-heptopyranose 7-Phosphate (36)

A suspension of furanose **34** (14 mg, 18 µmol) and 10% Pd/C (2 mg) in EtOH/EtOAc/H_2O (1.5:0.9:0.6, 3 mL) was stirred under H_2 atmosphere (1 bar) at r.t. for 16 h. The reaction mixture was filtered through a syringe filter and the filter was additionally washed with HPLC grade H_2O (10 mL). Et_3N (10 µL, 72 µmol) was added to the filtrate and the filtrate was concentrated until no solvent except H_2O were present. The remaining solution was passed through a short PD-10 column (HPLC grade H_2O). Product-containing fractions were pooled and lyophilized to give the 1,2-acetonide **35** as the triethylammonium salt; colorless solid (9.6 mg, 99%). Further processing was performed in two batches.

Batch 1: The phosphate **35** (4 mg, 7.9 µmol) was dissolved in deionized H_2O (2.6 mL) and rinsed through a short column of Dowex H$^+$. TFA (260 µL) was added to the filtrate and the solution was stirred for 12 h at r.t. The solution was co-evaporated with H_2O three times until no more TFA was present. Et_3N (20 µmol, 2.8 µL) was added and the mixture was again co-evaporated with H_2O (2 × 5 mL). The residue was taken up in H_2O (0.5 mL) and purified via gel chromatography (P-2, H_2O). Product-containing fractions were pooled and lyophilized to give the target compound as the free acid; white foam (2.5 mg, 99%).

Batch 2: The previous phosphate (4.7 mg, 9.3 µmol) was dissolved in deionized H_2O (3 mL) and rinsed through a short column of Dowex H$^+$, TFA (300 µL) was added and the reaction mixture was stirred for 12 h. The mixture was co-evaporated with H_2O three times until no more TFA was present. Et_3N (20 µmol, 2.8 µL) was added and the mixture was again co-evaporated with H_2O (2 × 5 mL). The residue was taken up in H_2O (0.5 mL) and purified via gel chromatography (P-2, H_2O). Product-containing fractions were pooled and lyophilized to give the target compound **36** as the free acid; white foam (2.7 mg, 99%). Both batches were combined (5.2 mg); $[\alpha]_D^{21}$ +17.6 (*c* 0.5, H_2O).

^{1}H NMR (600 MHz, D_2O): δ (α-anomer) = 5.18 (d, $J_{1,2}$ = 3.8 Hz, 1 H, H-1α), 4.08 (ddd, $J_{7b,6}$ = 7.4 Hz, $J_{7a,6}$ = 3.6 Hz, 1 H, H-6), 3.95 (ddd, $J_{7a,7b}$ = 11.7 Hz, $J_{7a,P}$ = 5.0 Hz, $J_{7a,6}$ = 3.9 Hz, 1 H, H-7a), 3.89 (dd, $J_{5,4}$ = 10.1 Hz, $J_{5,6}$ = 3.0 Hz, 1 H, H-5), 3.82 (ddd, $J_{7b,P}$ = 2.3 Hz, $J_{7b,6}$ = 7.2 Hz, $J_{7a,7b}$ = 11.7 Hz, 1 H, H-7b), 3.65 (app t, $J_{3,2} \cong J_{3,4} \cong J$ = 9.4 Hz, 1 H, H-3α), 3.56 (dd, $J_{3,4}$ = 8.9 Hz, $J_{4,5}$ = 10.2 Hz, 1 H, H-4), 3.52 (dd, *J* = 3.8, 9.8 Hz, 1 H, H-2),

^{1}H NMR (600 MHz, D_2O): δ (β-anomer) = 4.58 (d, *J* ≅ 8 Hz, 1 H, H-1 β), 4.11 (ddd, $J_{7b,6}$ = 7.1 Hz, $J_{7a,6}$ = 3.7 Hz, 1 H, H-6), 3.94 (ddd, $J_{7a,7b}$ = 11.7 Hz, $J_{7a,P}$ = 4.6 Hz, 1 H, H-7a), 3.83 (ddd, $J_{7b,P}$ = 2.3 Hz, 1 H, H-7b), 3.57 (dd, $J_{3,4}$ = 8.9 Hz, $J_{4,5}$ = 10.0 Hz, 1 H, H-4), 3.51 (dd, $J_{6,5}$ = 3.1 Hz, $J_{5,4}$ = 10.1 Hz, 1 H, H-5), 3.43 (t, *J* = 9.0 Hz, 1 H, H-3), 3.22 (dd, $J_{2,3}$ = 9.5 Hz, $J_{1,2}$ = 7.9 Hz, 1 H, H-2).

^{13}C NMR (150 MHz, D_2O): δ = 96.96 (C-1β), 92.82 (C-1α), 76.97 (C-5β), 76.66 (C-3β), 74.88 (C-2β), 73.74 (C-3α), 72.23 (C-2α), 72.15 (C-5α), 72.04 ($J_{P,C}$ = 6.6 Hz, C-6α), 71.73 ($J_{P,C}$ = 6.4 Hz, C-6β), 71.09 (C-4α), 70.97 (C-4β), 65.23 ($J_{P,C}$ = 5.1 Hz, C-7α), 64.94 ($J_{P,C}$ = 5.1 Hz, C-7β).

^{31}P NMR (242 MHz, D_2O): δ = 4.30.

LC-MS: *m*/*z* [M – H]$^-$ calcd for $C_7H_{15}O_{10}P$: 289.033; found: 289.0334.

N-Benzyloxycarbonyl-1,5-dideoxy-1,5-imino-D-glucitol (38)

To a solution of deoxynojirimycin hydrochloride (**37**; 1,5-dideoxy-1,5-imino-D-glucitol hydrochloride, 780 mg, 4 mmol) in MeOH/H_2O (3:2, 55 mL) at 0 °C was added $NaHCO_3$ (1.8 g, 0.02 mol) and then benzyl chloroformate (0.7 mL, 4.8 mmol) was added dropwise. The mixture was allowed to warm to r.t. and was stirred until complete conversion (2 h) as indicated by TLC (MeOH/EtOAc, 1:1). Detection was performed by spraying with ninhydrin stain followed by heating at 200 °C. The solvents were evaporated and the residue was partitioned between H_2O (60 mL) and EtOAc (40 mL). The organic phase was separated and the aqueous phase was reextracted with EtOAc (3 × 25 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The residue was chromatographed on silica gel (EtOAc → EtOAc/MeOH, 1:1) to give **38** as a colorless syrup (763 mg, 67%).

^{1}H NMR data were in agreement with those reported.[23]

2,3,4-Tri-*O*-benzyl-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-D-glucitol (39)

To a solution of **38** (757 mg, 2.55 mmol) in anhyd pyridine (27 mL) were added DMTrCl (1.55 g, 4.59 mmol) and DMAP (27 mg, 0.2 mmol) under argon and the mixture was stirred at r.t. for 5 h. Then EtOAc (3 mL) was added and the solution was washed with sat. aq $NaHCO_3$ (30 mL) and H_2O (30 mL). The aqueous phase was extracted with EtOAc (3 × 30 mL). The combined organic layers were dried ($MgSO_4$) and concentrated. The residue was dried under vacuum and then dissolved in anhyd DMF (45 mL). The solution was cooled to 0 °C (ice/water bath) and NaH (60% in mineral oil, 0.816 g, 0.02 mol) was added. After a few minutes, benzyl bromide (2.44 mL, 0.02 mol) was added dropwise over a 10 min period. The mixture was stirred for 2 h at r.t. under argon, and then cold H_2O (20 mL) was added. The mixture was extracted with Et_2O (3 × 5 mL). The combined organic phases were washed with H_2O, dried ($MgSO_4$), filtered, and concentrated. A solution of the residue in 80% aq AcOH (30 mL) was stirred at r.t. for 2.5 h. After concentration and coevaporation with toluene (3 ×), the residue was chromatographed on silica gel (EtOAc/hexane, 1:9 → 3:7) to afford **39** (820 mg, 57%) as a colorless oil; $[\alpha]_D^{21}$ –0.9 (*c* 0.7, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.35–7.26 (m, 15 H, ArH), 5.11 (br s, 2 H, CH_2, Cbz), 4.76–4.59 (m, 5 H, OCH_2Ph), 4.50 (d, part B of AB system, H-b, 1 H, $J_{a,b}$ = 11.7, OCH_2Ph), 4.00–3.79 (m, 3 H, H-5, H-6a, H-6b), 3.76–3.58 (m, 5 H, H-2, H-3, H-4, H-1a, H-1b).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.8 (C=O), 138.2, 138.1, 136.4 (q, ArC), 128.6, 128.6, 128.5, 128.5, 128.2, 128.1, 128.0, 127.9, 127.9, 127.9, 127.9, 127.8 (ArCH), 82.3 (C-3), 77.6 (C-4), 75.6 (C-2), 73.6, 73.4, 71.4 (3 × OCH_2Ph), 67.6 (CH_2, Bn, Cbz), 61.6 (C-6), 59.1 (C-5), 43.1 (C-1).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{35}H_{37}NO_6$: 568.2694; found: 568.2641.

2,3,4-Tri-*O*-benzyl-*N*-benzyloxycarbonyl-1,5,6,7-tetradeoxy-1,5-imino-D-*gluco*-hept-6-enopyranose (40)

DMSO (1.38 mmol, 0.1 mL) was added dropwise to a solution of oxalyl chloride (1.15 mmol, 0.57 mL, 2 M in CH_2Cl_2) in CH_2Cl_2 (6 mL) at –70 °C. After stirring for 10 min, a solution of **39** (650 mg, 1.15 mmol) in CH_2Cl_2 (6 mL) was added dropwise. The mixture was stirred for 1 h at –70 °C and then Et_3N (0.35 mL, 2.53 mmol) was added dropwise. After 5 min, the reaction was left to warm up to r.t. and stirred until complete conversion (ca. 1 h). Then H_2O was added and the aqueous

layer was extracted with EtOAc (3 ×). The combined organic layers were washed with H_2O, dried ($MgSO_4$), and concentrated. The crude aldehyde was dried in vacuum.

n-BuLi (2.76 mmol, 1.1 mL) was added to a suspension of methyltriphenylphosphonium bromide (2.87 mmol, 1.03 g) in THF (4 mL) under argon at 0 °C and the mixture was then stirred at r.t. for 1 h. A solution of the crude aldehyde in THF (4 mL) was added dropwise at –70 °C. The solution was stirred at –60 °C for 1 h, then allowed to warm to r.t., and stirred overnight. After cooling to 0 °C, H_2O was added, and the aqueous layer was extracted with EtOAc (3 ×). The combined organic phases were washed with brine, dried ($MgSO_4$), and concentrated. The residue was purified by chromatography on silica gel (EtOAc/hexane, 1:9) to afford the alkene **40** (400 mg, 62%) as a colorless oil; $[\alpha]_D^{22}$ +22.4 (*c* 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.22 (m, 15 H, ArH), 5.88 (ddd, $J_{6,5}$ = 5.3 Hz, $J_{6,7a}$ = 9.9 Hz, $J_{6,7b}$ = 16.7 Hz, 1 H, H-6), 5.22–5.10 (m, 4 H, H-7a, H-7b, CH_2, Cbz), 4.76 (dd, $J_{6,5}$ = 5.3 Hz, $J_{5,4}$ = 4.7 Hz, 1 H, H-5), 4.71–4.46 (m, 6 H, 3 × OCH_2Ph), 3.95 (dd, $J_{1a,1e}$ = 13.9 Hz, $J_{1a,2}$ = 6.0 Hz, 1 H, H-1a), 3.78–3.67 (m, 2 H, H-2, H-3), 3.58 (br t, $J_{3,4}$ = 4.4 Hz, $J_{4,5}$ = 4.7 Hz, 1 H, H-4), 3.44 (dd, $J_{1e,2}$ = 2.9 Hz, 1 H, H-1e).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.3 (C=O), 138.3, 138.1, 136.9 (q, ArC), 134.9 (C-6), 128.5, 128.5, 128.5, 128.0, 127.9, 127.9, 127.8, 127.7 (ArCH), 116.1 (C-7), 80.5 (C-3), 78.4 (C-4), 77.4 (C-2), 72.8, 72.4, 71.2 (OCH_2Ph), 67.4 (OCH_2Ph, Cbz), 57.5 (C-5), 40.7 (C-1).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{36}H_{37}NO_5$: 564.2744; found: 564.2724.

2,3,4-Tri-*O*-benzyl-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-D/L-*glycero*-D-*gluco*-heptitol (41a, 41b)

To a solution of alkene **40** (158 mg, 0.28 mmol) in 2:1 THF/H_2O (9 mL) was added *N*-methylmorpholine *N*-oxide (65 mg, 0.55 mmol). After stirring at r.t. for 10 min, OsO_4 (cat. amount) was added and the mixture was stirred for 1 h until complete conversion as observed by TLC (EtOAc/hexane, 1:1). Then sat. aq $Na_2S_2O_5$ (10 mL) was added. The mixture was extracted with EtOAc (3 × 10 mL). The organic phase was washed with 1 M aq HCl (10 mL), sat. aq $NaHCO_3$ (10 mL) and brine (15 mL), and dried ($MgSO_4$). After filtration and evaporation of volatiles, the crude was purified by chromatography on silica gel (hexane/EtOAc, 1:1) to afford the diol mixture **41a**/**41b** as a colorless oil (162 mg, 97%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38–7.18 (m, 20 H, ArH), 5.21–5.02 (m, 2 H, CH_2, Cbz), 4.76–4.40 (m, 6 H, OCH_2Ph), 4.29 (br t, *J* = 4.0 Hz, H-5), 4.25–4.16 (m, 1.5 H, H-5, H-6), 3.95–3.43 (m, 6.5 H, H-1a, H-2, H-3, H-4, H-6, H-7a, H-7b), 3.33 (dd, $J_{1a,1b}$ = 13.4 Hz, $J_{1b,2}$ = 2.9 Hz, 1 H, H-1b).

HRMS (ESI): *m*/*z* [M + HCOO]$^-$ calcd for $C_{36}H_{39}NO_7$: 642.2709; found: 642.2722.

2,3,4-Tri-*O*-benzyl-*N*-benzyloxycarbonyl-7-*O*-(*tert*-butyldiphenylsilyl)-1,5-dideoxy-1,5-imino-D-*glycero*-D-*gluco*-heptitol (42) and 2,3,4-Tri-*O*-benzyl-*N*-benzyloxycarbonyl-7-*O*-(*tert*-butyldiphenylsilyl)-1,5-dideoxy-1,5-imino-L-*glycero*-D-*gluco*-heptitol (44)

To a solution of **41a** and **41b** (0.162 g, 0.27 mmol) in anhyd CH_2Cl_2 (3.5 mL) was added imidazole (60 mg, 0.87 mmol). The solution was cooled to 0 °C and TBDPSCl (0.13 mL, 0.49 mmol) was added. The reaction mixture was stirred at 0–10 °C for 2 h, then diluted with CH_2Cl_2, and washed with H_2O. The aqueous phase was extracted with CH_2Cl_2 (3 ×). The combined organic layers were dried ($MgSO_4$). After filtration and evaporation of volatiles, the crude was purified by chromatography on silica gel (hexane/EtOAc, 7:1) to afford the 7-*O*-silylated derivatives **42** and **44** as colorless oils (216 mg, 95%, ratio 1.6:1).

Major Diastereoisomer 42

R_f = 0.18 (EtOAc/hexane, 1:7); $[\alpha]_D^{22}$ +2.0 (*c* 1.0, $CHCl_3$).

^{1}H NMR (600 MHz, toluene-d_8, 75 °C): δ = 7.74–7.70 (m, 4 H, ArH), 7.24–7.00 (m, 26 H, ArH), 5.06 (d, part A of AB system, *J* = 12.4 Hz, 1 H, OCH_2, Cbz), 4.99 (d, part B of AB system, *J* = 12.4 Hz, 1 H, OCH_2, Cbz), 4.67–4.38 (m, 6 H, H-5, 2 × OCH_2Ph, 1 × OCH_2Ph), 4.36–4.24 (m, 2 H, H-6, 1 × OCH_2Ph), 4.20 (t, $J_{3,4}$ = $J_{4,5}$ = 4.3 Hz, 1 H, H-4), 4.14–4.01 (m, 1 H, H-1a), 3.98–3.85 (m, $J_{6,7a}$ = 3.9 Hz, $J_{6,7b}$ = 7.7 Hz, $J_{7a,7b}$ = 10.7 Hz, 2 H, H-7a, H-7b), 3.83 (t, $J_{2,3}$ = 4.3 Hz, $J_{3,4}$ = 4.3 Hz 1 H, H-3), 3.56–3.51 (m, 1 H, H-2), 3.27 (br d, $J_{1a,1b}$ = 13.9 Hz, 1 H, H-1b), 1.14 [s, 9 H, C$(CH_3)_3$].

^{13}C NMR (150 MHz, toluene-d_8, 75 °C): δ = 156.6 (C=O), 139.4, 139.3, 139.0, 137.8, 136.1, 134.1 (q, ArC), 130.0, 129.2, 128.6, 128.6, 128.5, 128.5, 128.3, 128.2, 128.1, 128.0, 127.5, 127.5 (ArCH), 80.2 (C-3), 76.9 (C-2), 74.3 (C-4), 73.2 (*C*H_2Ph), 72.3 (*C*H_2Ph, C-6), 71.3 (*C*H_2Ph), 67.5 (*C*H_2Ph), 67.1 (C-7), 57.5 (C-5), 41.7 (C-1), 27.4 [C(*C*$H_3)_3$], 19.6 [*C*$(CH_3)_3$].

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{52}H_{57}NO_7Si$: 836.3977; found: 836.3955.

Minor Diastereoisomer 44

R_f = 0.10 (EtOAc/hexane, 1:7); $[\alpha]_D^{20}$ +1.7 (*c* 0.7, $CHCl_3$).

^{1}H NMR (600 MHz, toluene-d_8, 75 °C): δ = 7.77–7.70 (m, 4 H, C_6H_5), 7.28–6.93 (m, 26 H, C_6H_5), 5.02 (d, part A of AB system, *J* = 12.5 Hz, 1 H, CH_2, Cbz), 4.94 (d, part B of AB system, 1 H, CH_2, Cbz), 4.66 (s, 2 H, OCH_2Ph), 4.56–4.43 (m, 4 H, H-5, 1 × OCH_2Ph, 1 × OCH_2Ph), 4.29 (d, *J* = 11.6 Hz, 1 H, OCH_2Ph), 4.21–4.14 (m, 1 H, H-6), 3.98 (dd, $J_{6,7a}$ = 4.0 Hz, $J_{7a,7b}$ = 10.7 Hz, 1 H, H-7a), 3.88 (dd, $J_{6,7b}$ = 6.0 Hz, 1 H, H-7b), 3.82 (t, $J_{3,4}$ = $J_{4,5}$ = 6.0 Hz, 1 H, H-4), 3.72 (dd, $J_{2,3}$ = 5.1 Hz, $J_{3,4}$ = 6.0 Hz, 1 H, H-3), 3.62–3.53 (m, 3 H, H-2, H-1a, H-1b), 1.13 [s, 9 H, C$(CH_3)_3$].

^{13}C NMR (150 MHz, toluene-d_8, 75 °C): δ = 157.3 (C=O), 139.4, 139.3, 139.2, 137.8, 134.4, 134.2 (q, ArC), 130.1, 129.3, 128.7, 128.6, 128.5, 128.5, 128.3, 128.3, 127.8, 127.6 (ArCH), 82.6 (C-3), 78.6 (C-2), 76.8 (C-4), 73.9 (*C*H_2Ph), 73.6 (*C*H_2Ph), 71.9 (C-6), 71.5 (*C*H_2Ph), 67.7 (*C*H_2Ph, Cbz), 66.9 (C-7), 58.7 (C-5), 43.7 (C-1), 27.4 [C(*C*$H_3)_3$] and 19.7 [*C*$(CH_3)_3$].

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{52}H_{57}NO_7Si$: 836.3977; found: 836.3945.

Mosher's Esters 43 and 45

To a solution of (*S*)-(+)-α-methoxy-α-trifluoromethylphenylacetyl chloride (0.034 mmol, 6 µL) in anhyd pyridine (0.7 mL) and CCl_4 (0.5 mL) was added a solution of alcohol **44** (minor diastereoisomer, 13 mg, 0.016 mmol) in anhyd pyridine (1.2 mL). Then DMAP (cat. amount) was added and the mixture was stirred at 60 °C under argon for 2 d. Et_2NH (0.05 mol, 5 µL) was added and the mixture was partitioned between Et_2O (2 mL) and H_2O (6 mL). The organic layer was separated, washed with sat. aq NH_4Cl, and dried ($MgSO_4$). After filtration and evaporation of volatiles, the crude was purified by chromatography on silica gel (hexane/EtOAc, 7:1) to afford the MTPA-derivative **45** as a colorless oil (6 mg, 38%) along with recovered starting material **44** (5.6 mg, 43%).

^{1}H NMR (600 MHz, $CDCl_3$): δ (2 rotamers) = 7.69–6.88 (m, 29 H, ArH), 5.84 and 5.80 (ddd, 1 H, H-6 rotamers), 4.95–4.31 (m, 8 H, OCH_2Ph, Cbz), 4.59 and 4.54 (m, 1 H, H-5 rotamers), 4.27 and 3.97 (dd, H-1a rotamers), 3.95 and 3.85 (m, 2 H, H-7a, H-7b rotamers), 3.65–3.54 (m,

H-3 rotamers), 3.59 and 3.52 (s, 3 H, OCH_3 rotamers), 3.34 and 3.23 (br ddd, 1 H, H-2 rotamers), 3.32–3.27 (m, 1 H, H-4 rotamers), 2.83 and 2.77 (br d, 1 H, H-1e rotamers), 1.04 and 0.97 [s, 9 H, $C(CH_3)_3$, rotamers].

A similar procedure was applied to the major diastereoisomer **42** (13 mg), which gave 4 mg of the ester **43** (25%) with recovery of starting material **42** (7 mg, 65%).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.63–7.02 (m, 29 H, ArH), 5.92 (ddd, J = J = 4.0 Hz, J = 7.3 Hz, J = 7.3 Hz, 1 H, H-6), 5.05 (d, part A of AB system, $J_{a,b}$ = 12.2 Hz, 1 H, CH_2, Cbz), 4.96 (d, part B of AB system, 1 H, OCH_2Ph), 4.62–4.28 (m, 7 H, OCH_2Ph, H-5), 4.04 (br d, 1 H, H-1a), 3.88–3.74 (m, 2 H, H-7a, H-7b), 3.69 (t, $J_{2,3}$ = $J_{3,4}$ = 4.1 Hz, 1 H, H-3), 3.63 (t, $J_{3,4}$ = $J_{4,5}$ = 4.8 Hz, 1 H, H-4), 3.47 (br ddd, 1 H, H-2), 3.37 (s, 3 H, OCH_3), 2.83 (br d, 1 H, H-1b), 0.99 [s, 9 H, $C(CH_3)_3$].

2,3,4-Tri-*O*-benzyl-7-*O*-(*tert*-butyldiphenylsilyl)-5-*N*,6-*O*-carbonyl-1,5-dideoxy-1,5-imino-D-*glycero*-D-*gluco*-heptitol (46) and 2,3,4,7-Tetra-*O*-benzyl-5-*N*,6-*O*-carbonyl-1,5-dideoxy-1,5-imino-D-*glycero*-D-*gluco*-heptitol (47)

NaH (60% suspension in mineral oil; 31 mg, 0.08 mmol) was added to a solution of **42** (30 mg, 0.04 mmol) in anhyd DMF (1 mL) at 0 °C. After a few min, benzyl bromide (0.02 mL, 0.17 mmol) was added dropwise. The mixture was stirred overnight at r.t. under argon, and then cold H_2O (2 mL) was added. The mixture was extracted with Et_2O (3 × 1 mL). The combined organic phases were washed with H_2O and dried ($MgSO_4$). After filtration and concentration, the residue was subjected to column chromatography (EtOAc/hexane, 1:11 → 1:6) to give **46** (10 mg, 38%) and **47** (10 mg, 47%) as a syrup.

46

R_f = 0.2 (EtOAc/hexane, 1:3); $[\alpha]_D^{20}$ +19 (*c* 0.2, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.71–7.61 (m, 4 H, C_6H_5), 7.44–7.13 (m, 19 H, C_6H_5), 6.92–6.85 (m, 2 H, C_6H_5), 5.01 (d, part A of AB system, J = 10.8 Hz, 1 H, OCH_2Ph), 4.86 (d, part A of AB system, J = 11.1 Hz, 1 H, OCH_2Ph), 4.75–4.59 (m, 4 H, H-6, 1 × OCH_2Ph, 1 × OCH_2Ph), 4.15 (dd, $J_{1a,2}$ = 4.8 Hz, $J_{1a,1b}$ = 12.8 Hz, 1 H, H-1a, 1 × OCH_2Ph), 4.10–4.02 (m, $J_{6,7a}$ = 2.5 Hz, $J_{7a,7b}$ = 11.8 Hz, 2 H, H-7a), 3.84–3.65 (m, 3 H, $J_{6,7b}$ = 4.4 Hz, H-4, H-5, H-7b), 3.63–3.50 (m, 2 H, H-2, H-3), 2.74 (dd, $J_{1a,1b}$ = 12.8 Hz, $J_{1b,2}$ = 9.8 Hz, H-1b), 1.05 [s, 9 H, $C(CH_3)_3$].

^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.6 (C=O, Cbz), 86.8 (C-3), 77.5 (C-2), 76.7, 76.2 (C-4, C-6), 75.6 (CH_2Ph), 74.2 (CH_2Ph), 73.1 (CH_2Ph), 62.6 (C-7), 58.4 (C-5), 43.0 (C-1), 27.0 [$C(CH_3)_3$], 19.3 [$C(CH_3)_3$].

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{45}H_{49}NO_6Si$: 728.3402; found: 728.3403.

47

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.26 (m, 18 H, C_6H_5), 7.14–7.06 (m, 2 H, C_6H_5), 5.02 (d, part A of AB system, J = 10.8 Hz, 1 H, OCH_2Ph), 4.98 (d, part A of AB system, J = 11.1 Hz, 1 H, OCH_2Ph), 4.77–4.62 (m, 4 H, H-6, 1 × OCH_2Ph, 1 × OCH_2Ph), 4.54 (d, part A of AB system, J = 12.2 Hz, 1 H, OCH_2Ph), 4.48 (d, part B of AB system, 1 H, OCH_2Ph), 4.38 (d, part B of AB system, 1 H, OCH_2Ph), 4.15 (dd, $J_{1a,2}$ = 4.9 Hz, $J_{1a,1e}$ = 12.9 Hz, 1 H, H-1a), 3.83–3.66 (m, $J_{6,7a}$ = 3 Hz, $J_{7a,7b}$ = 11.3 Hz, 3 H, H-5, H-4, H-7a), 3.64–3.50 (m, 3 H, H-2, H-3, H-7b), 2.74 (dd, $J_{1a,1b}$ = 12.9 Hz, $J_{1b,2}$ = 10.1 Hz, 1 H, H-1b).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.5 (C=O), 138.3, 138.1, 137.8, 137.5 (Cq, C_6H_5), 128.7, 128.7, 128.6, 128.6, 128.1, 128.1, 128.0, 128.0, 128.0, 127.9, 127.6 (CH, C_6H_5), 86.9 (C-3), 77.6 (C-2), 76.4 (C-4), 75.8 (CH_2Ph), 75.3 (C-6), 74.2 (CH_2Ph), 74.0 (CH_2Ph), 73.2 (CH_2Ph), 68.0 (C-7), 58.5 (C-5), 43.0 (C-1).

2,3,4-Tri-*O*-benzyl-7-*O*-(*tert*-butyldiphenylsilyl)-5-*N*,6-*O*-carbonyl-1,5-dideoxy-1,5-imino-L-*glycero*-D-*gluco*-heptitol (48)

NaH (60% suspension in mineral oil; 0.8 mg, 0.002 mmol) was added to a solution of **44** (9 mg, 0.01 mmol) in anhyd DMF (2 mL) at 0 °C. After a few min, benzyl bromide (0.005 mL, 0.04 mmol) was added dropwise. The mixture was stirred overnight at r.t. under argon. Additional NaH (1 mg) and benzyl bromide (5 μL) were added and the reaction stopped after 3 additional h. Cold H_2O (2 mL) was added, the mixture extracted with Et_2O (3 × 2 mL). The combined organic phases were washed with H_2O and dried ($MgSO_4$). After filtration and concentration, the residue was subjected to column chromatography (EtOAc/hexane, 1:10 → 1:5) to give **48** (2.6 mg, 37%) as a syrup; R_f = 0.34 (EtOAc/hexane, 1:3); $[\alpha]_D^{23}$ +0.5 (*c* 1.0, $CHCl_3$).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.65–7.61 (m, 4 H, C_6H_5), 7.45–7.13 (m, 21 H, C_6H_5), 5.00 (d, J = 10.6 Hz, 1 H, CH_2Ph), 4.89 (d, J = 11.6 Hz, 1 H, CH_2Ph), 4.82 (d, J = 10.6 Hz, 1 H, CH_2Ph), 4.72–4.66 (m, 2 H, CH_2Ph), 4.59 (d, J = 11.6 Hz, 1 H, CH_2Ph), 4.17 (dd, $J_{2,1e}$ = 5.3 Hz, $J_{1a,1e}$ = 13.2 Hz, 1 H, H-1e), 3.94 (dd, J = 7.1 Hz, 3.5 Hz, 1 H, H-6), 3.79 (dd, $J_{6,7a}$ = 3.0 Hz, $J_{7b,7a}$ = 11.5 Hz, 1 H, H-7a), 3.61–3.53 (m, 3 H, H-2, H-3, H-7b), 3.49 (dd, $J_{6,5}$ = 4.2 Hz, $J_{4,5}$ = 9.6 Hz, 1 H, H-5), 3.32 (app t, $J_{3,4}$ ~ $J_{4,5}$ = 9.6 Hz, 1 H, H-4), 2.75 (dd, $J_{2,1a}$ = 1.9 Hz, $J_{1a,1e}$ = 13.2 Hz, 1 H, H-1a), 1.02 [s, 9 H, $C(CH_3)_3$].

^{13}C NMR (150 MHz, $CDCl_3$): δ = 156.03 (C=O), 138.23, 137.72, 137.69 (Cq, C_6H_5), 135.67, 135.55 (CH, C_6H_5), 132.95, 132.57 (Cq, TBDPS), 129.89, 129.87, 128.56, 128.54, 128.45, 128.14, 128.11, 127.97, 127.93, 127.83, 127.81, 127.78 (CH, C_6H_5), 85.99 (C-3), 79.66 (C-4), 77.74 (C-6), 77.64 (C-2), 75.88, 74.97, 73.17 (CH_2Ph), 64.25 (C-7), 57.56 (C-5), 42.60 (C-1), 26.66 [$C(CH_3)_3$], 19.23 [$C(CH_3)_3$].

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{45}H_{49}NO_6Si$: 728.3402; found: 728.3412.

2,3,4-Tri-*O*-benzyl-*N*-benzyloxycarbonyl-1,5-dideoxy-1,5-imino-L-*glycero*-D-*gluco*-heptitol (41b)

HF·pyridine (70% solution, 1.2 mL) was added to a solution of **44** (30 mg, 0.065 mmol) in THF (2.5 mL) at r.t. The solution was stirred for 5 h, then the reaction was quenched with sat. aq $NaHCO_3$ and extracted with EtOAc (3 ×). The combined organic phases were dried ($MgSO_4$) and concentrated. Purification of the residue on silica gel (hexane/EtOAc, 1:1) afforded **41b** (21 mg, 98%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.37–7.17 (m, 20 H, ArH), 5.19–5.04 (m, 2 H, OCH_2, Cbz), 4.77–4.52 (m, 5 H, 2 × OCH_2Ph, 1 × OCH_2Ph, Cbz), 4.44 (d, J = 11.9 Hz, 1 H, OCH_2Ph), 4.30 (br t, J = 3.7 Hz, 1 H, H-5), 4.02 (br d, J = 13.6 Hz, 1 H, H-1a), 3.95–3.85 (m, 1 H, H-6), 3.82–3.64 (m, 3 H, $J_{3,4}$ = 7.3 Hz, $J_{4,5}$ = 3.4 Hz, H-2, H-3, H-4), 3.63–3.38 (m, 3 H, H-1b, H-7a, H-7b).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 79.9 (C-3), 76.6 (C-4), 75.7 (C-2), 72.6 (C-6), 63.4 (C-7), 56.5 (C-5), 42.5 (C-1).

HRMS (ESI): *m*/*z* [M + HCOO]$^-$ calcd for $C_{36}H_{39}NO_7$: 642.2709; found: 642.2722.

1,5-Dideoxy-1,5-imino-L-*glycero*-D-*gluco*-heptitol Hydrochloride (49)

The benzylated iminosugar **41b** (22 mg, 0.037 mmol) was dissolved in anhyd THF (2.5 mL). Then a catalytic amount (spatula tip) of 10% Pd/C was added and the suspension was stirred under H_2 atmosphere for 48 h. The suspension was then filtered, washed with MeOH (3 ×) and concentrated in vacuo. The residue was dissolved in H_2O (HPLC grade) and subjected to gel filtration using a PD-10 Sephadex G 25 column (H_2O). The eluate was lyophilized. The solid residue was dissolved in H_2O and applied on a column of Dowex 50W-X8 resin (H^+-form). The

column was washed with H_2O, and the product was eluted with aq 1 M NH_4OH. Product-containing fractions were concentrated, and then lyophilized.

^{1}H NMR (300 MHz, MeOD): δ = 3.95 (td, $J_{5,6}$ = 2.4 Hz, $J_{6,7a}$ ~ $J_{6,7b}$ = 5.8 Hz, 1 H, H-6), 3.69–3.63 (m, 2 H, H-7a, H-7b), 3.57 (ddd, $J_{2,3}$ = 8.9 Hz, $J_{2,1a}$ = 10.6 Hz, $J_{2,1e}$ = 5.1 Hz, 1 H, H-2), 3.36 (dd, $J_{3,4}$ = 9.0 Hz, $J_{4,5}$ = 9.6 Hz, 1 H, H-4), 3.20 (t, $J_{2,3}$ = $J_{3,4}$ = 8.9 Hz, 1 H, H-3), 3.06 (dd, part A of ABX, $J_{1e,2}$ = 5.1 Hz, $J_{1a,1e}$ = 12.7 Hz, 1 H, H-1e), 2.45 (dd, $J_{4,5}$ = 9.6 Hz, $J_{5,6}$ = 2.4 Hz, 1 H, H-5), 2.4 (dd, part B of ABX, $J_{1a,2}$ = 10.6 Hz, $J_{1a,1e}$ = 12.8 Hz, 1 H, H-1a).

H_2O (1 mL) and aq 1 M HCl (0.5 mL) were added to the freeze-dried material and the solution was stirred for 2 h at r.t. and then concentrated. The residue was applied on a column of Sephadex G-10 and the product was eluted with H_2O. After lyophilization, the target compound **49** was obtained as a white amorphous solid (4.4 mg, 52% overall yield); $[\alpha]_D^{22}$ +3 (*c* 0.2, H_2O).

^{1}H NMR (600 MHz, D_2O): δ = 4.07 (ddd, $J_{5,6}$ = 2.0 Hz, $J_{6,7a}$ = 7.4 Hz, $J_{6,7b}$ = 5.0 Hz, 1 H, H-6), 3.74–3.69 (m, $J_{6,7a}$ = 7.4 Hz, $J_{6,7b}$ = 5.1 Hz, $J_{7a,7b}$ = 11.7 Hz, 2 H, H-7a, H-7b), 3.51 (ddd, $J_{1e,2}$ = 5.1 Hz, $J_{2,3}$ = 9.0 Hz, $J_{1a,2}$ = 11.0 Hz, 1 H, H-2), 3.44–3.34 (m, 2 H, H-3, H-4), 3.12 (dd, $J_{1a,1b}$ = 12.7 Hz, $J_{1e,2}$ = 5.0 Hz, 1 H, H-1e), 2.55 (dd, $J_{4,5}$ = 9.6 Hz, $J_{5,6}$ = 1.9 Hz, 1 H, H-5), 2.44 (dd, $J_{1a,1e}$ = 12.8 Hz, $J_{1a,2}$ = 10.9 Hz, 1 H, H-1a).

^{13}C NMR (data from HSQC spectra, D_2O): δ = 78.4 (C-3), 71.4 (C-4), 71.0 (C-2), 69.1 (C-6), 63.9 (C-7), 60.0 (C-5), 48.3 (C-1).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_7H_{15}NO_5$: 194.1023; found: 194.1023; $[M + Na]^+$ calcd for $C_7H_{15}NO_5$: 216.0842; found: 216.0841.

Acknowledgment

The authors gratefully acknowledge financial support of this work by Mutabilis. Dr. Andreas Hofinger-Horvath is thanked for recording the NMR spectra and Hedda Drexler for measuring the HRMS data.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0036-1591518.

References

(1) New address: D. Atamanyuk, AB-Science, 3 Avenue George V, 75008, Paris, France.
(2) New address: N. M. Xavier, Center of Chemistry and Biochemistry, DQB, Faculdade de Ciências, Universidade de Lisboa, Ed. C8, 2º Piso, Campo Grande 1749-016 Lisboa, Portugal.
(3) New address: V. Gerusz, Debiopharm, Rue du Levant 146, CP368, 1920 Martigny, Switzerland.
(4) (a) Maxson, T.; Mitchell, D. A. *Tetrahedron* **2016**, *72*, 3609. (b) Chellat, M. F.; Raguž, L.; Riedl, R. *Angew. Chem. Int. Ed.* **2016**, *55*, 6600. (c) Walsh, C. *Nat. Rev. Microbiol.* **2013**, *1*, 65. (d) Schäberle, T. F.; Hack, I. M. *Trends Microbiol.* **2014**, *22*, 165. (e) Taylor, P. L.; Wright, G. D. *Anim. Health Res.* **2008**, *9*, 237.
(5) (a) Escaich, S. *Curr. Opin. Chem. Biol.* **2008**, *12*, 400. (b) Kuo, C.-J.; Chen, J.-W.; Chiu, H.-C.; Teng, C.-H.; Hsu, T.-I.; Lu, P.-J.; Syu, W.-J.; Wang, S.-T.; Chou, T.-C.; Chen, C.-S. *Frontiers Cell. Infect. Microbiol* **2016**, *6*, 82; doi: 10.3389/fcimb.2016.00082. (c) Loutet, S. A.; Flannagan, R. S.; Kooi, C.; Sokol, P. A.; Valvano, M. *J. Bacteriol.* **2006**, *188*, 2073.
(6) For example, see: (a) Reinhardt, A.; Wehle, M.; Geissner, A.; Crouch, E.; Kang, Y.; Yang, Y.; Anish, C.; Santer, M.; Seeberger, P. H. *J. Struct. Biol.* **2016**, *195*, 387. (b) Gomery, K.; Müller-Loennies, S.; Brooks, C. L.; Brade, L.; Kosma, P.; Di Padova, F.; Brade, H.; Evans, S. V. *Proc. Natl. Acad. Sci. U.S.A.* **2012**, *109*, 20877. (c) Wang, H.; Head, J.; Kosma, P.; Brade, H.; Müller-Loennies, S.; Sheikh, S.; McDonald, B.; Smith, K.; Cafarella, T.; Seaton, B.; Crouch, E. *Biochemistry* **2008**, *47*, 710. (d) Marchetti, R.; Malinovska, L.; Lameignère, E.; Adamova, L.; De Castro, C.; Cioci, G.; Stanetty, C.; Kosma, P.; Molinaro, A.; Wimmerova, M.; Imberty, A.; Silipo, A. *Glycobiol.* **2012**, *22*, 1387.
(7) Raetz, C. R.; Whitfield, C. *Annu. Rev. Biochem.* **2002**, *71*, 635.
(8) Holst, O. In *Bacterial lipopolysaccharides*; Knirel, Y. A.; Valvano, M., Eds.; Springer: Wien, **2011**, 21.
(9) Kosma, P. *Curr. Org. Chem.* **2008**, *12*, 1021.
(10) (a) Butty, F.; Aucoin, M.; Morrison, L.; Ho, N.; Shaw, G.; Creuzenet, C. *Biochemistry* **2009**, *48*, 7764. (b) McCallum, M.; Shaw, S. D.; Shaw, G. S.; Creuzenet, C. *J. Biol. Chem.* **2012**, *287*, 29776.
(11) (a) Lu, Q.; Yao, Q.; Xu, Y.; Li, L.; Li, S.; Liu, Y.; Gao, W.; Niu, M.; Sharon, M.; Ben-Nissan, G.; Zamyatina, A.; Liu, X.; Chen, S.; Shao, F. *Cell Host Microbe* **2014**, *16*, 351. (b) Yao, Q.; Lu, Q.; Wan, X.; Song, F.; Xu, Y.; Hu, M.; Zamyatina, A.; Liu, X.; Huang, N.; Zhu, P.; Shao, F. *eLife* **2014**, *3*, e03714; doi: 10.7554/eLife.03714. (c) Benz, I.; Schmidt, M. A. *Mol. Microbiol.* **2001**, *40*, 1403.
(12) (a) Eidels, L.; Osborn, M. J. *Proc. Natl. Acad. Sci. U.S.A.* **1971**, *68*, 1673. (b) Valvano, M.; Messner, P.; Kosma, P. *Microbiol.* **2002**, *148*, 1979; and references cited therein. (c) For the expansion of the abbreviations, see: Kneidinger, B.; Marolda, C.; Graninger, M.; Zamyatina, A.; McArthur, F.; Kosma, P.; Valvano, M.; Messner, P. *J. Bacteriol.* **2002**, *184*, 363.
(13) Gaudet, R. G.; Sintsova, A.; Buckwalter, C. M.; Leung, N.; Cochrane, A.; Li, J.; Cox, A.; Moffat, J.; Gray-Owen, S. D. *Science* **2016**, *348*, 1251.
(14) Zamyatina, A.; Gronow, S.; Oertelt, C.; Puchberger, M.; Brade, H.; Kosma, P. *Angew. Chem. Int. Ed.* **2000**, *39*, 4150.
(15) (a) Yu, C.-K.; Wang, C.-J.; Chew, Y.; Wang, P.-C.; Yin, H.-S.; Kao, M.-C. *Biochem. Biophys. Res. Commun.* **2016**, *477*, 794. (b) Do, H.; Yun, J.-S.; Lee, C. W.; Choi, Y. J.; Kim, H.-Y.; Kim, Y.-J.; Park, H.; Chang, J. H.; Lee, J. H. *Mol. Cells* **2015**, *38*, 1086. (c) Taylor, P. L.; Blakeley, K. M.; de Leon, G. P.; Walker, J. R.; McArthur, F.; Evdokimova, E.; Zhang, K.; Valvano, M. A.; Wright, G. D.; Junop, M. S. *J. Biol. Chem.* **2008**, *283*, 2835. (d) Harmer, N. J. *Mol. Biol.* **2010**, *400*, 379. (e) Vivoli, M.; Isupov, M. N.; Nocholas, R.; Hill, A.; Scott, A. E.; Kosma, P.; Prior, J. L.; Harmer, N. J. *Chem. Biol.* **2015**, *22*, 1622.
(16) Coleman, W. G.; Leive, L. *J. Bacteriol.* **1979**, *139*, 899.
(17) (a) Taylor, P. L.; Blakeley, K. M.; de Leon, G. P.; Walker, J. R.; McArthur, F.; Evdokimova, E.; Zhang, K.; Valvano, M. A.; Wright, G. D.; Junop, M. S. *J. Biol. Chem.* **2008**, *283*, 2835. (b) Desroy, N.; Denis, A.; Oliveira, C.; Atamanyuk, D.; Briet, S.; Faivre, F.; Le Fralliec, G.; Bonvin, Y.; Oxoby, M.; Escaich, S.; Floquet, S.; Drocourt, E.; Vongsouthi, V.; Durant, L.; Moreau, F.; Verhey, T. B.; Lee, T.-W.; Junop, M. S.; Gerusz, V. *J. Med. Chem.* **2013**, *56*, 1418. (c) Lee, T.; Verhey, T. B.; Antiperovitch, P. A.; Atamanyuk, D.; Desroy, N.; Oliveira, C.; Denis, A.; Gerusz, V.; Drocourt, E.; Loutet, S. A.; Hamad, M. A.; Stanetty, C.; Andres, S. N.; Sugiman-Marangos, S.; Kosma, P.; Valvano, M.; Moreau, F.; Junop, M. S. *J. Med. Chem.* **2013**, *56*, 1405. (d) De Leon, G. P.; Elowe, N. H.; Koteva, K. P.; Valvano, M. A.; Wright, G. D. *Chem. Biol.* **2006**, *13*, 437.

(18) Durka, M.; Tikad, A.; Périon, R.; Bosco, M.; Andaloussi, M.; Floquet, S.; Malacain, E.; Moreau, F.; Oxoby, M.; Gerusz, V.; Vincent, S. P. *Chem. Eur. J.* **2011**, *17*, 11305.
(19) Brimacombe, J. S.; Kabir, A. K. M. S. *Carbohydr. Res.* **1986**, *150*, 35.
(20) Zamyatina, A.; Puchberger, M.; Graziani, A.; Gronow, S.; Hofinger, A.; Kosma, P. *Carbohydr. Res.* **2003**, *338*, 2571.
(21) Richtmyer, N. K.; Carr, C. J.; Hudson, C. S. *J. Am. Chem. Soc.* **1943**, *65*, 1477.
(22) Bannwarth, W.; Trzeciak, A. *Helv. Chim. Acta* **1987**, *70*, 175.
(23) Wessel, H.-P.; Iversen, T.; Bundle, D. R. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2247.
(24) Khanna, I. K.; Koszyk, F. J.; Stealey, M. A.; Weier, R. M.; Julien, J.; Mueller, R. A.; Rao, S. N.; Swenton, L. *J. Carbohydr. Chem.* **1995**, *14*, 843.
(25) Cha, J. K.; Christ, W. J.; Kishi, Y. *Tetrahedron* **1984**, *40*, 2247.
(26) (a) Van Straten, N. C. R.; Kriek, N. M. A. J.; Timmers, C. M.; Wigchert, S. C. M.; van der Marel, G. A.; van Boom, J. H. *J. Carbohydr. Chem.* **1997**, *16*, 947. (b) Crich, D.; Banerjee, A. *Org. Lett.* **2005**, *7*, 1395.
(27) Chan, T.-H.; Chang, Y.-F.; Hsu, J.-J.; Cheng, W.-C. *Eur. J. Org. Chem.* **2010**, 5555.
(28) Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512.
(29) Lauritsen, A.; Madsen, R. *Org. Biomol. Chem.* **2006**, *4*, 2898.
(30) Lundt, I.; Madsen, R. *Synthesis* **1995**, 787.
(31) (a) Desroy, N.; Moreau, F.; Briet, S.; Le Fralliec, G.; Floquet, S.; Durant, L.; Vongsouthi, V.; Gerusz, V.; Denis, A.; Escaich, S. *Bioorg. Med. Chem.* **2009**, *17*, 1276. (b) Gerusz, V.; Vincent, S.; Oxoby, M.; Atamanyuk, D.; Moreau, F.; Andaloussi, M.; Tikad, A. Patent PCT Int. Appl. WO 2012/073214 A2, **2012**.
(32) See, for example: (a) Stütz, A. E. *Iminosugars as Glycosidase Inhibitors: Nojirimycin and Beyond*; Wiley-VCH: Weinheim, **1999**. (b) Zou, W. *Curr. Top. Med. Chem.* **2005**, *5*, 1363. (c) Asano, N. *Glycobiol.* **2003**, *13*, 93R.
(33) Dhavale, D. D.; Kumar, K. A. A.; Chaudhari, V. D.; Sharma, T.; Sabharwal, S. G.; Reddy, J. P. *Org. Biomol. Chem.* **2005**, *3*, 3720.
(34) Harris, R. K.; Becker, E. D.; Cabral de Menezes, S. M.; Goodfellow, R.; Granger, P. *Pure Appl. Chem.* **2001**, *73*, 1795.