Iminosugars as glucosylceramide processing enzymes inhibitors: design, synthesis and evaluation

Liu, B.

6 Synthesis and Biological Evaluation of *N*-substituted α-Geminal Bis-hydroxymethyl Piperidine Iminosugars

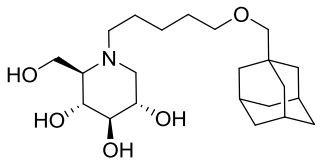
Introduction

Deoxynojirimycin (DNJ) and its congeners are inhibitors of a wide variety of glycosidases as well as some glycosyltransferases. *N*-alkyl DNJ derivatives have been identified as compounds with considerable therapeutic potential for the treatment of various diseases including diabetes and several lysosomal storage disorders (LSDs). Two characteristic iminosugars often included in studies aimed for the design of glycoprocessing enzymes are the natural product, DNJ, and its C-5 epimer, L-*ido*-DNJ.[1] *N*-butyl-DNJ is a moderately potent

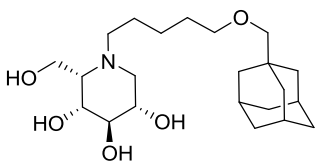
glucosylceramide synthase (GCS) inhibitor and based on this virtue used in the clinic for the treatment of Gaucher disease in what is termed substrate reduction therapy. Enlarging the substituent on the DNJ nitrogen improves GCS inhibitory potency, but at the same time results in more potent off-target inhibition. Similarly substituted, L-*ido*-configured iminosugars appear to be much cleaner: they inhibit GCS with equal or (slightly) superior potency compared to their DNJ counterparts and are, with the exception of neutral glucosylceramidase (GBA2), remarkably more selective. These observations invite the question, which underlies the work described in this Chapter, whether hybrid piperidines bearing two α-geminal hydroxymethyl moieties (thus featuring both DNJ and L-*ido*-DNJ hydroxymethyls) would be valid GCS inhibitors, and if so, would be (even) more selective than existing *N*-alkyl-iminosugars.

Figure 1 depicts the lead-iminosugars that led to the studies described here. *N*-AMP-DNJ (**1**, MZ-21) is a potent GCS/GBA1/GBA2 inhibitor, and its L-*ido* congener (**2**, MZ-31), has (slightly) improved GCS/GBA2 inhibitory potency offset by considerable loss in GBA1 inhibitory activity. *N*-AMP D-*galacto* DNJ (**3**) and *N*-AMP L-*altro* DNJ (**4**) are the C-4 epimers of *N*-AMP DNJ and *N*-AMP L-*ido*-DNJ, respectively. Compound **3** is a moderately potent GCS inhibitor and a potent GBA2 inhibitor, and intestinal glycosidases are also inhibited by this compound. Epimer **4** in contrast is only a moderate GBA2 inhibitor with low or no inhibition of intestinal glycosidases, GCS and GBA1.

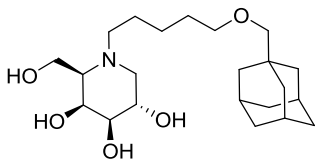
***Figure 1**: IC50 values of N-AMP DNJ isosteres for GlcCer metabolizing enzymes*



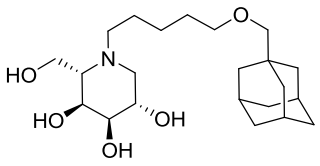
1, MZ-21 IC_{50} GCS 200 nM
IC_{50} GBA1 0.1 μM
IC_{50} GBA2 2 nM



2, MZ-31 IC_{50} GCS 100 nM
IC_{50} GBA1 30 μM
IC_{50} GBA2 1 nM



3 *IC_{50} GCS 500 nM
*IC_{50} GBA1 0.2 μM
*IC_{50} GBA2 <1 nM

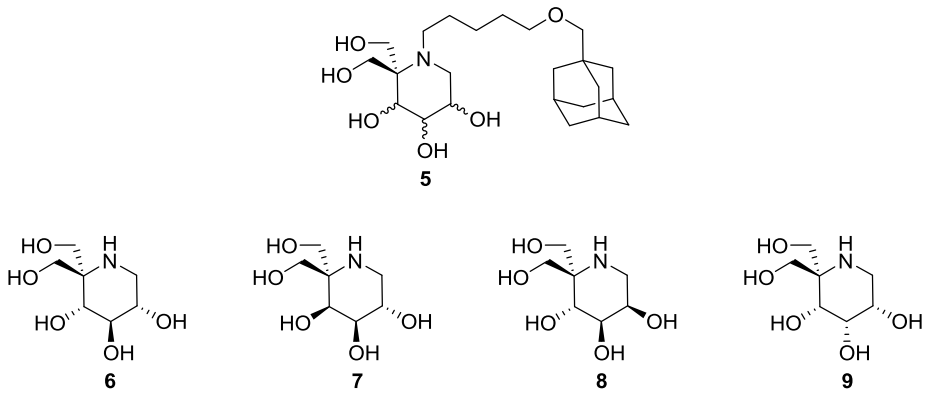


4 *IC_{50} GCS >100 μM
*IC_{50} GBA1 30 μM
*IC_{50} GBA2 500 nM

*IC_{50} data from Wennekes *el al.*[1]

These findings led to the design of a number of hybrid iminosugars bearing two geminal hydroxymethyl substituents, as depicted in Figure 2. The list of target compounds encompasses the configurational D-*gluco*-L-*ido* (**6**) and D-*galacto*-L-*altro* (**7**) pairs, but also a choice number of compounds emulating in configuration other pyranosides and that may be of interest in their own right (**8**, **9** and their *N*-alkyl derivatives).

Figure 2: *Structures of N-AMP α-geminal bishydroxymethyl iminosugars*

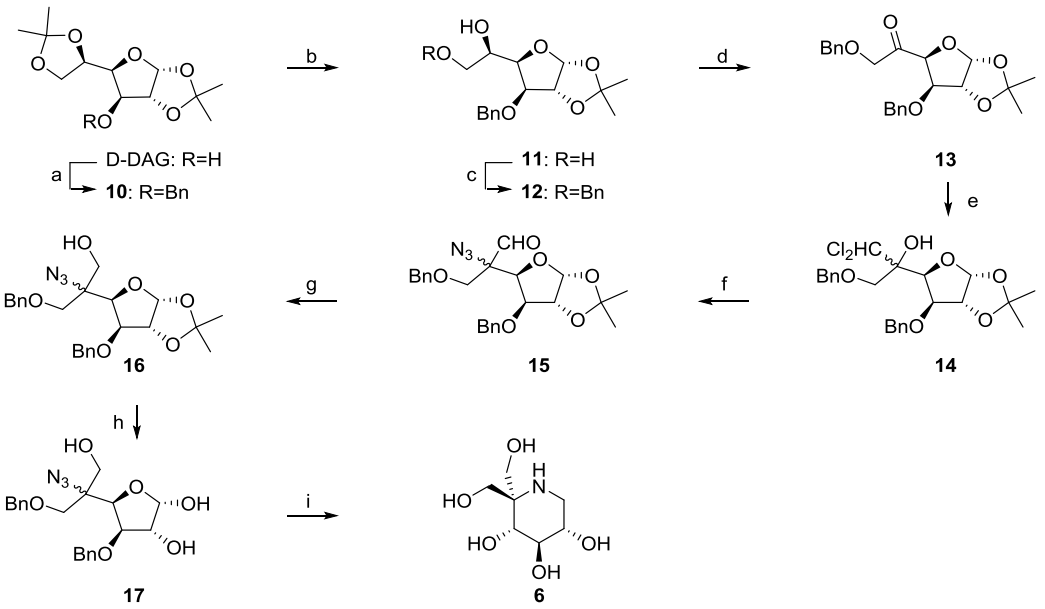


Results and discussion

Synthesis of 5-*C*-hydroxymethyl-DNJ (6)

Pawar *et al.* documented the synthesis of α-geminal bishydroxymethyl piperidines, which was adopted in the synthesis of D-*gluco*-L-*ido* configured compounds **6** and its C-2 and C-3 epimers.[2] In the first instance, the synthesis of D-*gluco*-L-*ido* DNJ (**6**) was undetaken following the literature procedure (Scheme 1).[2] Correspondingly, D-diacetone glucose (D-DAG) was treated with sodium hydride and benzyl bromide to give **10**. Protonolysis of **10** afforded diol **11**. Regioselective benzylation under the agency of dibutyltin oxide, sodium hydride and benzyl bromide afforded **12** in high yield. The secondary alcohol in **12** was oxidized using PCC to yield ketone **13**. *In situ* formation of dichloromethane carbanion, from dichloromethane and lithium di-isopropyl amide, and subsequent addition to ketone **13** afforded methylene dichloride **14**. An α-azido group was introduced at C-5 in **14** via a Jocic Reeve reaction to give **15**. Azido-aldehyde **15** was reduced using sodium borohydride to afford azido alcohol **16**. Demasking of the isopropylidene protecting group, followed by hydrogenation and subsequent reductive amination yielded the target α-geminal bishydroxymethyl DNJ **6** in an overall yield of 6%.

***Scheme 1**: Synthesis of 5-C-hydroxymethyl-1-deoxynojirimycin (**6**)*



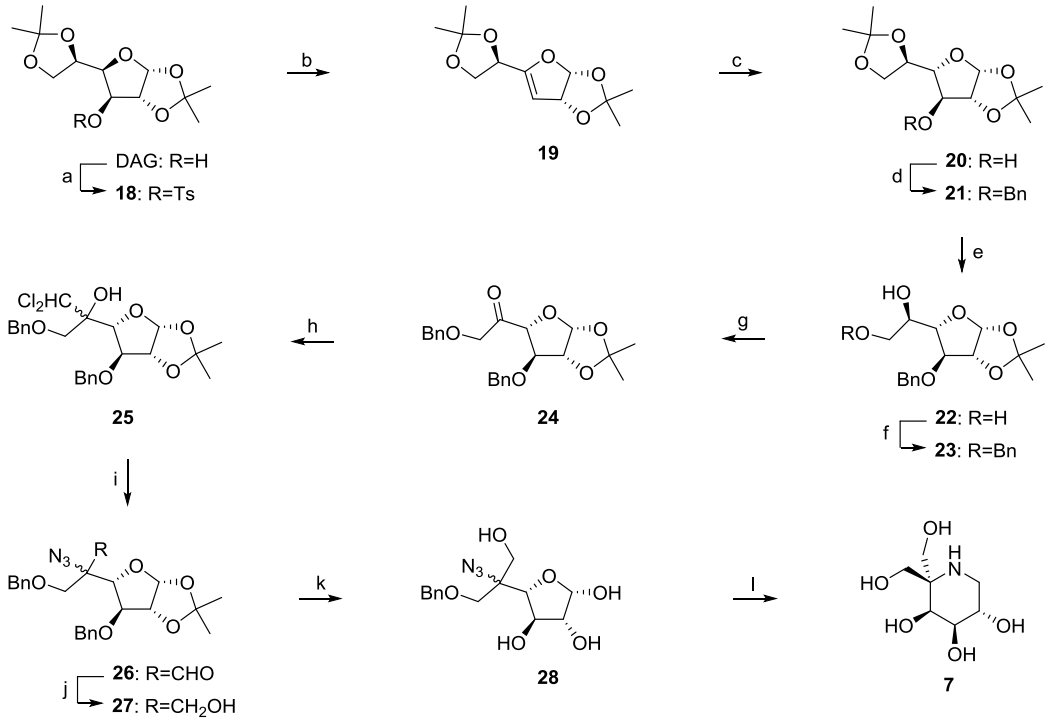
Reagents and conditions: [**a**] NaH, BnBr, DMF, 97%; [**b**] AcOH, H_2O, 80%; [**c**] 1) Bu_2SnO, toluene, 2) NaH, BnBr, 90%; [**d**] PCC, DCM, 53%; [**e**] LDA, DCM, THF, 55%; [**f**] NaN_3, DMF, TBAI, 115 °C, 69%; [**g**] $NaBH_4$, 89%; [**h**] TFA, H_2O, 68%; [**i**] H_2, Pd/C, 5 bar, 74%.

Synthesis of 5-*C*-hydroxymethyl-1-deoxy-D-galactonojirimycin (7)

It was anticipated that the chemical transformation depicted in Scheme 1 could also be applied on the C-4 epimer of diacetone glucose: diacetone galactose, which would give access to D-*galacto*-L-*altro*-iminosugar **7**. Tosylation of DAG[3] and subsequent β-elimination of tosylate **18** gave glycal **19**[4] in high yield (Scheme 2). Hydroboration and subsequent diastereoselective oxidation afforded the desired diacetone galactose **20** in good yield.[5] Compound **20** was subjected to the transformations as outlined above for the synthesis of **6**. The hydroxyl functionality in **20** was protected using benzyl bromide to give **21**. Isopropylidene demasking of **21** with aqueous acidic acid afforded diol **22**. Regioselective benzylation with the aid of dibutyltin oxide afforded **23**. Alcohol **23** was oxidized with PCC to give ketone **24**. The key step in this synthesis is the introduction of dichloromethylene onto the 5-ketone **24** to form **25**, a reaction that proceeded in an even better yield than that on glucose isomer **14**. Compound **25** was next reacted with sodium azide in DMF at 115 °C to uneventfully give **26** in a yield of 93%. Aldehyde **26** was reduced to give alcohol **27**, which underwent a TFA-water hydrolysis to remove the isopropyl protecting group after which the resulting intermediate **28** was exposed

to 5 bar H_2 atmosphere and a catalytic amount of palladium on carbon to remove the benzyls, reduce the azide to the amine and effect an ensuing intramolecular reductive amination to yield target iminosugar **7** (12% over 12 steps).

***Scheme 2**: Synthesis of 5-C-hydroxymethyl-1-deoxy-D-galactonojirimycin (**7**)*

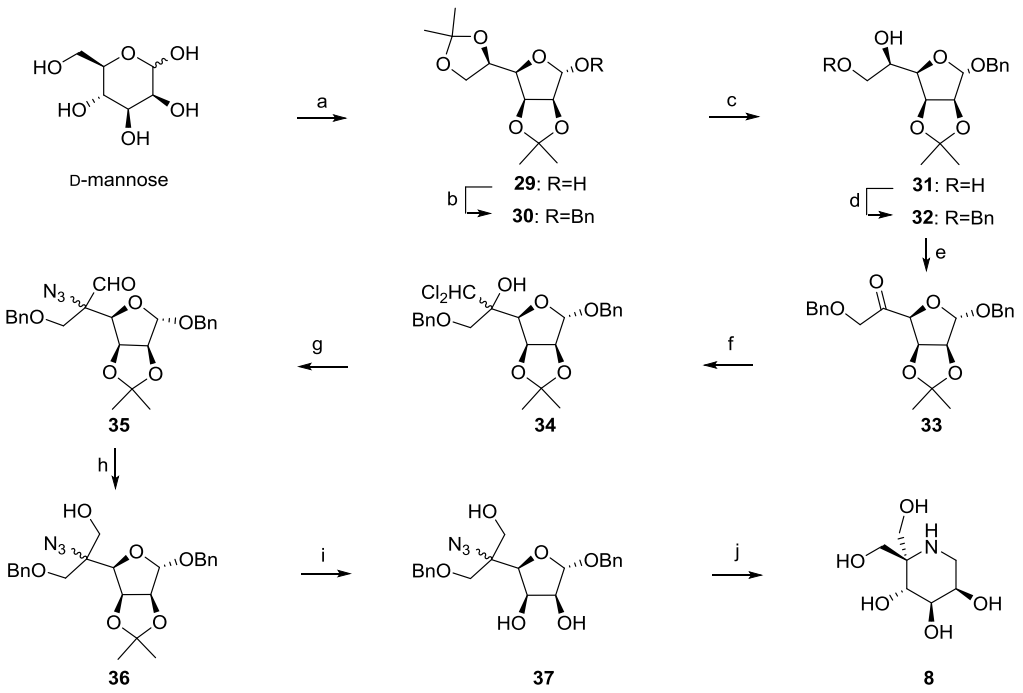


Reagents and conditions: [**a**] *p*-TsCl, pyridine, DCM, 60 °C, 98%; [**b**] *t*BuOK, THF, 0 °C, 91%; [**c**] 1) BH_3·THF, THF; 2) NaOH, H_2O_2, 75%; [**d**] NaH, BnBr, DMF; [**e**] AcOH, H_2O, 86%, 2 steps; [**f**] 1) Bu_2SnO, tol, 2)TBABr, BnBr, 82%; [**g**] PCC, DCM, 92%; [**h**] LDA, DCM, -78 °C, 74%; [**i**] NaN_3, TBAI, DMF, 115 °C, 93%; [**j**] $NaBH_4$, MeOH, 0 °C, 82%; [**k**] TFA, H_2O, 0 °C, 63%; [**l**] Pd/C, H_2, EtOH, 5 bar, 91%.

Synthesis of 5-*C*-hydroxymethyl-1-deoxy-D-mannonojirimycin (8) and 5-*C*-hydroxymethyl-1-deoxy-D-allonojirimycin (9)

The D-*manno*-L-*gulo* iminosugar **8** and D-*allo*-L-*talo* iminosugar **9** were synthesized as described by Pawar *et al.*[2] The synthesis of **8** starts with TBATB catalyzed isopropylidenation of D-mannose to give **29**.[6] Benzylation of **29** gained **30** and subsequent acidic hydrolysis of the acetal protecting group afforded **31**. Alcohol **31** underwent the 7-step transformation as described above for the preparation of **6** and **7**, which generated **8** in an overall yield of 9% (10 steps).

***Scheme 3**: Synthesis of 5-C-hydroxymethyl-1-deoxy-D-mannonojirimycin (**8**)*

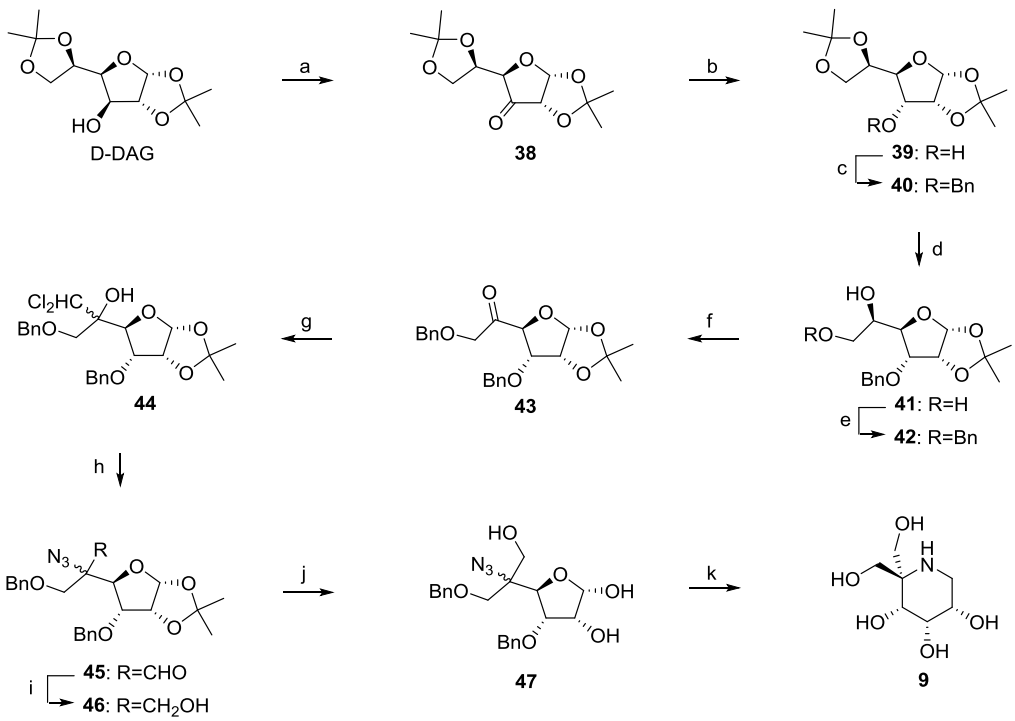


Reagents and conditions: [**a**] TBATB, acetone, 64%; [**b**] 18-crown-6, BnBr, KOH, THF, 75%; [**c**] AcOH, H_2O, r.t., 81%; [**d**] 1) Bu_2SnO, tol; 2) BnBr, TBABr, 76%; [**e**] PCC, DCM, 30 °C, 88%; [**f**] LDA, THF, -78 °C, 66%; [**g**] NaN_3, TBAI, DMF, 115 °C, 87%; [**h**] $NaBH_4$, MeOH, 0 °C, 80%; [**i**] TFA, H_2O, 0 °C, 45%; [**j**] Pd/C, H_2, EtOH, 5 bar, 82%.

In a similar vein, diacetone allose **39**, obtained via oxidation and stereoselective reduction from D-DAG, was transformed to produce compound **9** (Scheme 4). The C-3 alcohol of D-DAG was oxidized to form aldehyde **38**, which was reduced by sodium borohydride to give diacetone D-allose **39** in 74% yield over the 2 steps. Compound **9** was prepared from **39** as described previously for the synthesis of **6** with an overall yield of 9% in 9 steps.

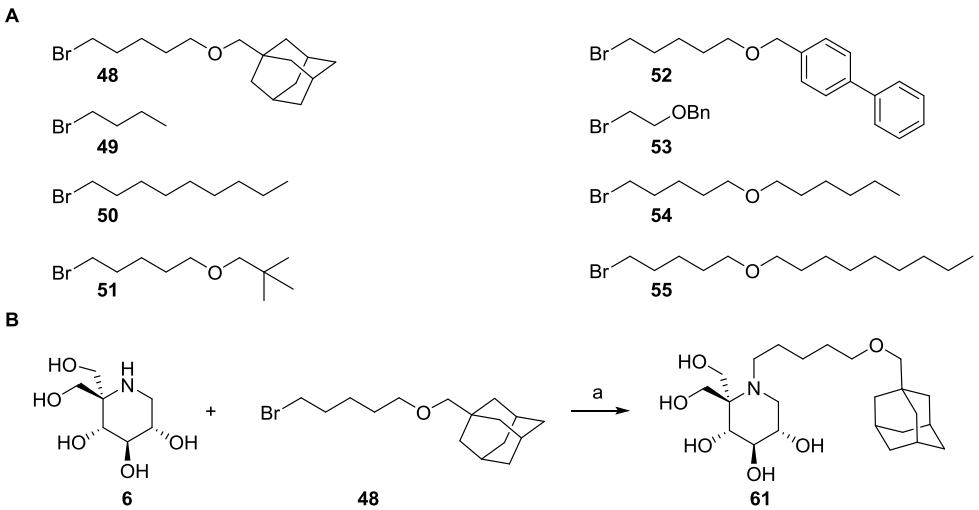
With the four α-geminal bis-(hydroxymethyl) piperidines (**6**, **7**, **8** and **9**) in hand, the target hydrophobic iminosugars were prepared by treating **6** - **9** with bromides **48** – **55** (Scheme 5A; see for the final structures Figures 4, 5, 6 and 7). As an example, the synthesis of *N*-AMP D-*gluco*-L-*ido* DNJ (**61**) is depicted in Scheme 5B. Treatment of D-*gluco*-L-*ido* DNJ (**6**) with bromide **48** and potassium carbonate in DMF gave **61** in 11% yield (Scheme 5B). Yields of the *N*-alkyl derivatives vary from 2% to 46% after HPLC purification (see the experimental section for details).

***Scheme 4**: 5-C-Hydroxymethyl-1-deoxy-D-allonojirimycin (**9**)*



Reagents and conditions: [**a**] PCC, DCM, 81%; [**b**] $NaBH_4$, EtOAc, H_2O, 92%; [**c**] NaH, BnBr, DMF, 90%; [**d**] AcOH, H_2O, 46%; [**e**] 1) Bu_2SnO, tol; 2) BnBr, TBABr, 76%; [**f**] PCC, DCM, 64%; [**g**] DCM, LDA, THF, -78 °C, 99%; [**h**] NaN_3, DMF, 115 °C, 71%; [**i**] $NaBH_4$, MeOH, 0 °C, 81%; [**j**] TFA, H_2O, 0 °C, 70%; [**k**] Pd/C, H_2, EtOH, 5 bar, 81%.

***Scheme 5**: N-alkylation of α-geminal hydroxymethyl iminosugars*

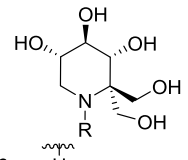


Reagents and conditions: [**a**] K_2CO_3, DMF, 80 °C, 11%.

Biological evaluation

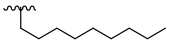
D-*Gluco*-L-*ido* hybrid iminosugars

Figure 3: *Enzyme inhibition assay results: IC_{50} values, for D-gluco-L-ido DNJ and its N-alkyl derivatives as inhibitors of GCS, GBA1 and GBA2, in comparision with the corresponding D-gluco-DNJ and L-ido-DNJ analogues*

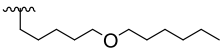


6 H
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 32 μM

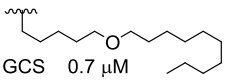
56
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 515 μM



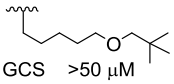
57
IC_{50} GCS 45 μM
IC_{50} GBA1 81 μM
IC_{50} GBA2 0.15 μM



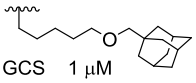
58
IC_{50} GCS 3.5 μM
IC_{50} GBA1 54 μM
IC_{50} GBA2 0.15 μM



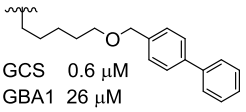
59
IC_{50} GCS 0.7 μM
IC_{50} GBA1 95 μM
IC_{50} GBA2 0.1 μM



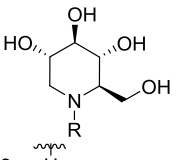
60
IC_{50} GCS >50 μM
IC_{50} GBA1 271 μM
IC_{50} GBA2 2 μM



61
IC_{50} GCS 1 μM
IC_{50} GBA1 8 μM
IC_{50} GBA2 0.03 μM

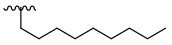


62
IC_{50} GCS 0.6 μM
IC_{50} GBA1 26 μM
IC_{50} GBA2 6 nM

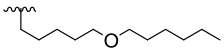


63 H
IC_{50} GCS >50 μM
IC_{50} GBA1 754 μM
IC_{50} GBA2 20 μM

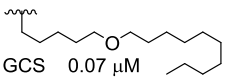
64
IC_{50} GCS 50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 0.3 μM



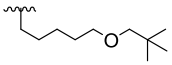
65
IC_{50} GCS 1.4 μM
IC_{50} GBA1 3 μM
IC_{50} GBA2 2 nM



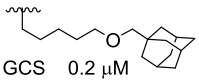
66
IC_{50} GCS 0.08μM
IC_{50} GBA1 5 μM
IC_{50} GBA2 2 nM



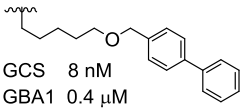
67
IC_{50} GCS 0.07 μM
IC_{50} GBA1 0.4 μM
IC_{50} GBA2 1.5 nM



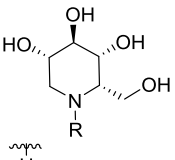
68
IC_{50} GCS 5 μM
IC_{50} GBA1 6 μM
IC_{50} GBA2 5 nM



1
IC_{50} GCS 0.2 μM
IC_{50} GBA1 0.5 μM
IC_{50} GBA2 0.8 nM

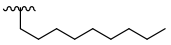


69
IC_{50} GCS 8 nM
IC_{50} GBA1 0.4 μM
IC_{50} GBA2 0.7 nM

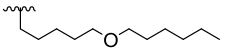


70 H
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 138 μM

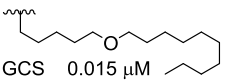
71
IC_{50} GCS 4 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 0.2 μM



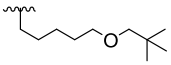
72
IC_{50} GCS 0.1 μM
IC_{50} GBA1 40 μM
IC_{50} GBA2 1 nM



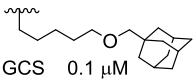
73
IC_{50} GCS 0.03 μM
IC_{50} GBA1 102 μM
IC_{50} GBA2 3 nM



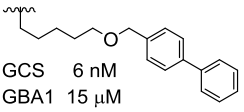
74
IC_{50} GCS 0.015 μM
IC_{50} GBA1 9 μM
IC_{50} GBA2 0.15 nM



75
IC_{50} GCS 1.6 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 10 nM



2
IC_{50} GCS 0.1 μM
IC_{50} GBA1 34 μM
IC_{50} GBA2 1 nM



76
IC_{50} GCS 6 nM
IC_{50} GBA1 15 μM
IC_{50} GBA2 1 nM

The D-*gluco*-L-*ido* iminosugars (**6**, **56** - **62**) were tested on their inhibitory potency against the glucosylceramide metabolizing enzymes, GCS, GBA1 and GBA2. The corresponding D-*gluco* (**1**, **63** - **69**) and L-*ido* (**2**, **70** - **76**) iminosugar derivatives were included as reference compounds to determine the effect of the additional hydroxymethyl group on the C-5 position. The results are tabulated in Figure 3. From the results it can be seen that the DNJ and L-*ido*-DNJ derivatives are without exception the more potent GCS inhibitors when compared with their D-*gluco*-L-*ido* configured α-geminal bishydroxymethyl piperidine counterparts, irrespective of the nature of the *N*-alkyl substituent. In line with what was reported previously the L-*ido* iminosugars proved to be the more potent GCS inhibitor when compared with the D-*gluco*-configured equivalent. Based on this result, it can be concluded that installment of an extra C-5 hydroxymethyl group at the carbon already bearing such a substituent is detrimental for GCS inhibition.

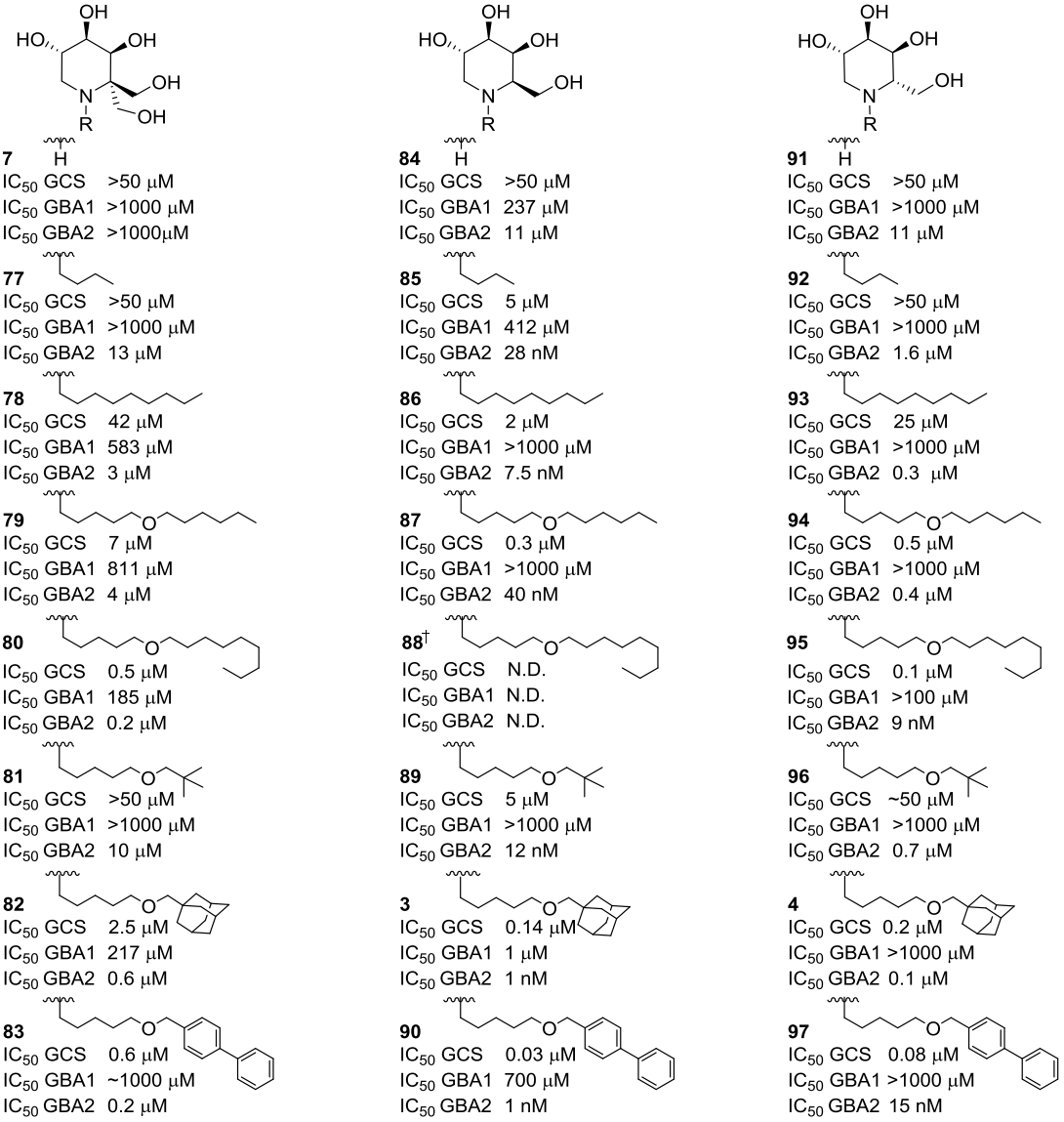
When looking at GBA1 inhibition values, it is remarkable that, whereas the hybrid iminosugars are all weaker inhibitors compared to the D-*gluco* configured molecules, they sometimes outperform their L-*ido* counterparts. This may indicate that the D-*gluco* configuration is preferred by GBA1, that an additional hydroxymethyl group may increase the steric hindrance and thus affect the inhibitory activity, but that this may be less detrimental than altering the configuration at C-5.

The effect of adding an extra hydroxymethyl at C-5 on GBA2 inhibition is as was noted for GCS inhibitory activity: the D-*gluco*-L-*ido* hybrid iminosugars are still relatively potent GBA2 inhibitors, but much less so than the corresponding D-*gluco* and L-*ido* compounds.

D-*Galacto*-L-*altro* hybrid iminosugars

In Figure 4, the inhibitory potencies towards GCS, GBA and GBA2 of the D-*galacto*-L-*altro* hybrid iminosugars (**7**, **77** - **83**) as well as that of their and the parent compounds (D-*galacto* isomers, **3**, **84** – **90**; L-*altro* isomers, **4**, **91** – **97**) are depicted. The D-*galacto*-L-*altro* hybrids do inhibit GCS to some extend, however not at the concentrations at which the D-*galacto* and L-*altro* iminosugars inhibit GCS. None of the compounds, with the exception of D-*galacto* AMP (**3**, IC_{50} GBA1 = 1 μM) inhibit GBA. In contrast, several of the D-*galacto* configured iminosugars inhibit GBA2 in the nanomolar range and are even more potent than the corresponding DNJ (i.e. **64**, **1** and **69**) and L-*ido*-DNJ derivatives (i.e. **71**, **2** and **76**). The D-*galacto*-L-*altro* hybrid compounds, though, are only weak GBA2 inhibitors, if at all, and also here it appears that the extra appendage at C-5 is detrimental for inhibition potency.

Figure 4: *Enzyme inhibition assay results: IC_{50} values, for D-galacto-L-altro-DNJ and its N-alkyl derivatives as inhibitors of GCS, GBA1 and GBA2, in comparision with the corresponding D-galacto-DNJ and L-altro-DNJ analogues*



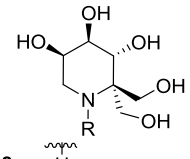
† : Compound not synthesized; N.D.: Activity not determined

D-*Manno*-L-*gulo* iminosugars

As shown in Figure 5, none of the D-*manno*-L-*gulo* hybrid iminosugars potently inhibit GCS. The most active GCS inhibitor in this series is the biphenyl derivative **104**. Remarkably, however, the hybrid molecules do sometimes outperform their D-*manno* and L-*gulo* configured

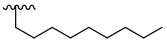
counterparts, in terms of GCS inhibitory potency (compare, for instance the GCS inhibitory potency of **102** with **110** and **118**, and **103** with **111** and **109**). The potency of this series as GBA1 and GBA2 inhibitors is modest at most.

Figure 5: *Enzyme inhibition assay results: IC_{50} values, for D-manno-L-gulo-DNJ and its N-alkyl derivatives as inhibitors of GCS, GBA1 and GBA2, in comparision with the corresponding D-manno-DNJ and L-gulo-DNJ analogues*

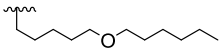


8 R = H
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 >1000 μM

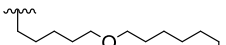
98
IC_{50} GCS 40 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 18 μM



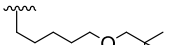
99
IC_{50} GCS >50 μM
IC_{50} GBA1 594 μM
IC_{50} GBA2 4 μM



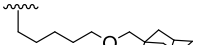
100
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 3 μM



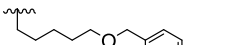
101
IC_{50} GCS >50 μM
IC_{50} GBA1 >200 μM
IC_{50} GBA2 25 μM



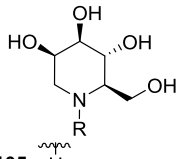
102
IC_{50} GCS 11 μM
IC_{50} GBA1 394 μM
IC_{50} GBA2 10 μM



103
IC_{50} GCS 13 μM
IC_{50} GBA1 389 μM
IC_{50} GBA2 3 μM

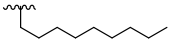


104
IC_{50} GCS 3 μM
IC_{50} GBA1 898 μM
IC_{50} GBA2 1 μM

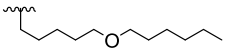


105 R = H
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 >100 μM

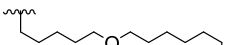
106
IC_{50} GCS ~10 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 >1000 μM



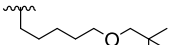
107
IC_{50} GCS >50 μM
IC_{50} GBA1 >100 μM
IC_{50} GBA2 >1000 μM



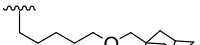
108
IC_{50} GCS 8 μM
IC_{50} GBA1 929 μM
IC_{50} GBA2 3 μM



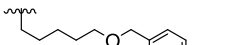
109
IC_{50} GCS >50 μM
IC_{50} GBA1 110 μM
IC_{50} GBA2 31 μM



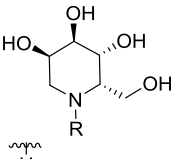
110
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 >1000 μM



111
IC_{50} GCS >50 μM
IC_{50} GBA1 62 μM
IC_{50} GBA2 61 μM

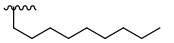


112
IC_{50} GCS 3 μM
IC_{50} GBA1 133 μM
IC_{50} GBA2 N.D.

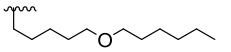


113 R = H
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 >1000 μM

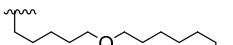
114
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 >1000 μM



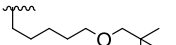
115
IC_{50} GCS >50μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 7.5 μM



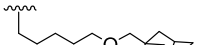
116
IC_{50} GCS 21 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 10 μM



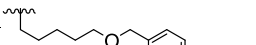
117
IC_{50} GCS 4 μM
IC_{50} GBA1 972 μM
IC_{50} GBA2 2 μM



118
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 42 μM



119
IC_{50} GCS >50 μM
IC_{50} GBA1 988 μM
IC_{50} GBA2 3 μM

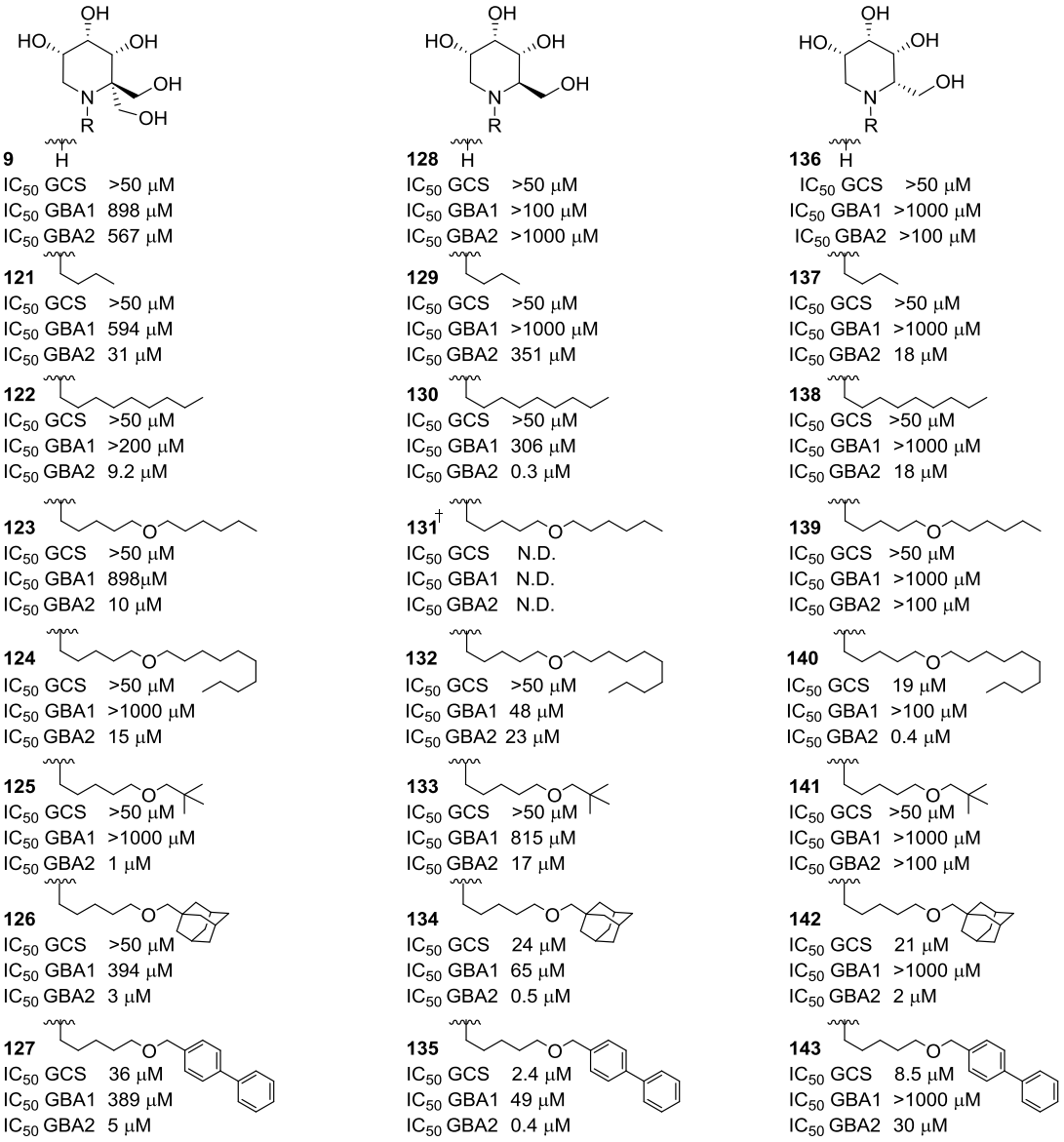


120†
IC_{50} GCS N.D.
IC_{50} GBA1 N.D.
IC_{50} GBA2 N.D.

† : Compound not synthesized; N.D.: Activity not determined

D-*Allo*-L-*talo* hybrid iminosugars

Figure 6: *Enzyme inhibition assay results: IC50 values, for D-allo-L-talo-DNJ and its N-alkyl derivatives as inhibitors of GCS, GBA1 and GBA2, in comparision with the corresponding D-allo-DNJ and L-talo-DNJ analogues*



† : Compound not synthesized; N.D.: Activity not determined

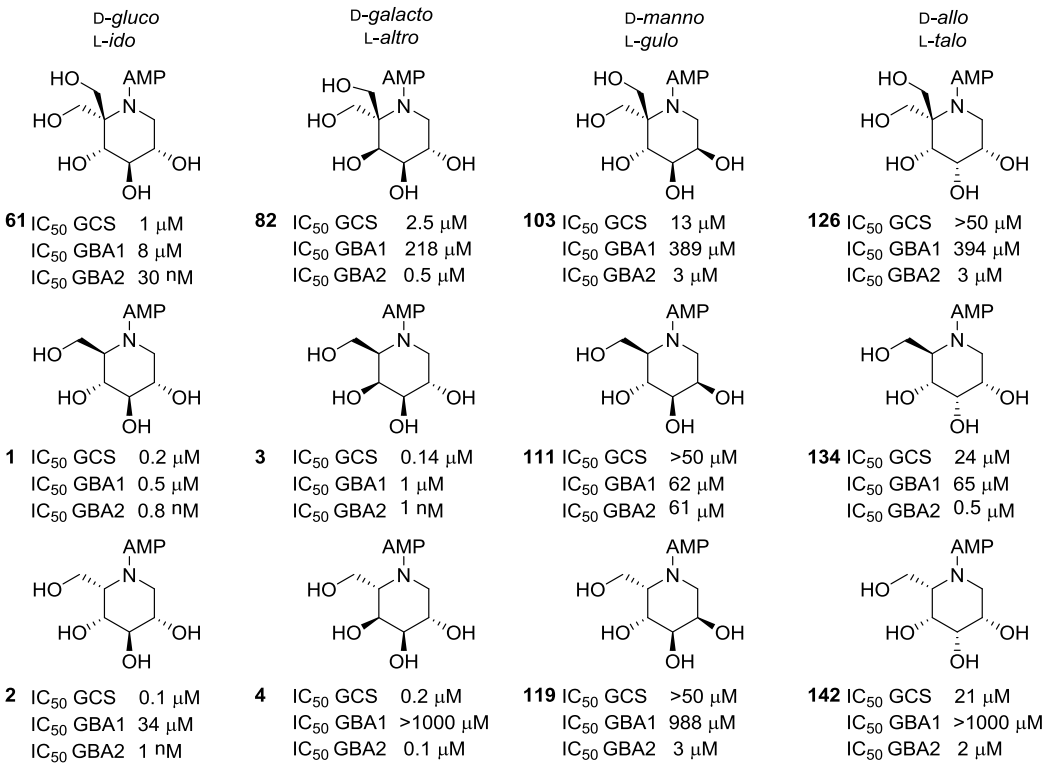
The results of the biological assays of the D-*allo*-L-*talo* hybrid iminosugar series (**9**, **121** - **127**), D-*allo* series (**128** - **135**) and L-*talo* series (**136** - **143**) are given in Figure 6. As can be

seen, the series contains no GCS/GBA/GBA2 inhibitors with remarkable potency. Obviously, the rather drastic deviation of the glucose configuration is detrimental for inhibition of the three glucose-processing enzymes, and addition of an extra hydroxymethyl does not help.

Conclusion

In this Chapter, iminosugars that encompass both the D-glucose and L-idose structural properties in one molecule as well as its C-2, C-3 and C-4 epimers were synthesized. These four sets of hybrid compounds (**6**, **7**, **8** and **9**) were *N*-alkylated with various hydrophobic substitutes which produced a library of 28 *N*-alkylated derivatives. This set and their corresponding DNJ congeners have been tested as inhibitors for the GlcCer metabolic enzymes (GCS, GBA1 and GBA2).

Figure 7: *Enzyme inhibition assay results: IC_{50} values of the N-AMP iminosugar derivatives*



Generally, the hybrid compounds are weaker GCS inhibitors compared to both D-configured and L-configured iminosugars (Figure 7), with the D-*manno*-L-*gulo* compound **103** being an exception. Concerning GBA1 inhibitory activity, the bis-hydroxymethyl compounds are

generally more potent than their corresponding L-compounds while less potent than the D-compounds. This may indicate that the D-configuration at C-5 is more beneficial for the iminosugar to bind to GBA1, and that an additional hydroxymethyl has a negative effect in binding to the active site of the enzyme. There is no specific rule observed for how the extra hydroxymethyl group affects GBA or GBA2 activity, and general trends appear the same as for GCS activity. It should be noted that many of the compounds described here are of a configuration that is rather far removed from that of glucopyranose. It may therefore well be that the compound collections may contain inhibitors for glycoprocessing enzymes other than those assayed here. It would therefore be of interest to screen the compound collections against other glycosidases, including galactosidases and mannosidases that are of interest in their own right in biological and biomedical research.

Experimental Section

Enzyme inhibition assays: The potencies (IC_{50} values) of the *N*-alkyl-DNJ derivatives as GCS, GBA1 and GBA2 inhibitors were determined by exposing cells or enzyme preparations to an appropriated range of iminosugar concentrations.

GCS: IC_{50} values for GCS activity were measured using living cells with NBD-ceramide as substrate.[7] Briefly, cells were incubated with 50 nmol C6-NBD-ceramide (6-[*N*-methyl-*N*-(7-nitrobenz-2-oxa-1,3-diazol-4-yl)aminododecanoyl]sphingosine) in the presence of increasing compound concentrations. The cells were harvested after 2h followed by lipid extraction. The formed C6-NBD-glucosylceramide was quantified using a Molecular Dynamics Typhoon phosphor imaging device. IC_{50} values were determined from the titration curves. The experiment was performed twice.

GBA1: IC_{50} values for lysosomal GBA1 were measured using 4-methylumbeliferyl-β-D-glucoside as substrate.[8] Briefly, recombinant GBA1 was incubated with increasing compound concentrations for 30 min at 0 °C. Enzyme activity was determined with 3.7 mM 4-methylumbelliferyl-β-D-glucopyranoside in McIlvaine buffer (0.1 M citrate and 0.2 M phosphate buffer), pH 5.2, 0.1% Triton X-100 (v/v) and sodium taurocholate (0.2%, w/v). Assays performed in triplicate were incubated at 37 °C for 30 min and quenched by the addition of glycine/NaOH (0.2 mL, pH 10.6). The amount of liberated 4-methylumbeliferyl was determined with a PerkinElmer Life Sciences LS30 fluorimeter, excitation wavelength 366 nm, emission wavelength 445 nm.

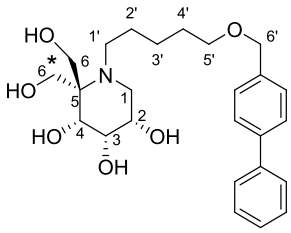
GBA2: IC_{50} values for the non-lysosomal glucocerebrosidase (GBA2) were measured with 4-methylumbeliferyl-β-D-glucoside as substrate.[8] GBA2-rich membrane suspensions were prepared from enzyme-overexpressing HEK cells by sonicating, and the suspension was pre-incubated for 30 min at 37 °C with conduritol-B-epoxide (1 mM, CBE, Sigma) to inhibit the lysosomal glucocerebrosidase (GBA1). The prepared GBA2-rich suspension was then incubated with increasing compound concentrations for another 30 min, and then incubated with 3.7 mM 4-methylumbeliferyl-β-D-glucoside in McIlvaine buffer (0.1 M citrate and 0.2 M phosphate buffer), pH 5.8. Assays were incubated at 37 °C for 1 hour and quenched by the addition of glycine/NaOH (0.2 mL, pH 10.6). The amount of liberated 4-methylumbeliferyl was determined

with a PerkinElmer Life Sciences LS30 fluorimeter, excitation wavelength 366 nm, emission wavelength 445 nm. Assays were performed in triplicate.

General compound synthesis, purification and analysis methods: All solvents and reagents were obtained commercially and used as received unless stated otherwise. Reactions were executed at room temperature unless stated otherwise. Moisture sensitive reactions were performed under argon atmosphere. Water was removed from starting compounds by repetitive coevaporation with toluene. Solvents were removed by evaporation under reduced pressure. DCM, DMF, and THF were dried over activated 4Å molecular sieves for at least 12 hours before use. Compounds were visualized during TLC analyses by UV (254 nm), and with the following staining solutions: aqueous solution of $KMnO_4$ (5 g/L) and K_2CO_3 (25 g/L). Visualization of hemiacetals and glycosides was achieved by spraying with a solution of 20% H_2SO_4 in ethanol followed by charring at ≈ 200 °C. Column chromatography purification was performed on silica gel (40-63 μm). ^1H and ^{13}C-APT NMR spectra were recorded on a Bruker AV 400 (400/100 MHz) or Bruker 600 (600/150 MHz) spectrometer in $CDCl_3$, MeOD or D_2O. Chemical shifts are given in ppm (δ) relative to TMS as internal standard (^1H NMR in $CDCl_3$) or the signal of the deuterated solvent.[9] Coupling constants (*J*) are given in Hz. High resolution mass spectra were recorded by direct injection (2 μL of a 2 μM solution in water/acetonitrile/*tert*-butanol 1:1:1 v/v/v) on a mass spectrometer (Thermo Finnigan LTQ Orbitrap) equipped with an electrospray ion source with resolution R = 60000 at m/z 400 (mass range m/z = 150-2000). IR spectra were recorded on a Shimadzu FTIR-8300 and are reported in cm^{-1}. Optical rotation were measured on an automatic polarimeter of sodium D-line, at λ = 589 nm. Size-exclusion purifications were performed on an ÄKTA-explorer, column size d = 26 mm, l = 60 mm, mobile phase NH_4HCO_3 (0.15 M) in H_2O, flow 1.5 mL/min. HPLC Purification were performed on a Prep LCMS, Gemini from Phenomenex B.V. (C-18, 110 Å, 5 μm, 19 x 150 mm column).

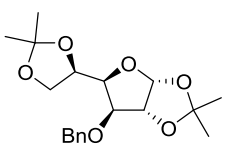
General Procedure: Alkylation of iminosugars. To a mixture of the bromide chain (0.3 mmol, see Scheme 5A) and K_2CO_3 (0.4 mmol) was added a solution of the 5-hydroxymethyl nojirimycin derivative (0.2 mmol) in DMF (1 mL). The reaction suspension was stirred at 80 °C overnight. After cooling to room temperature, the mixture was filtered and concentrated. The crude compound was purified with HPLC.

***Figure 8**: Proton and carbon NMR numbering of N-alkylated iminosugars*



Synthesis of 5-*C*-hydroxymethyl-1-deoxynojirimycin (6)

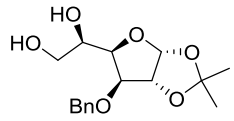
3-*O*-Benzyl-1,2:5,6-di-*O*-isopropylidene-α-D-*gluco*-furanoside (10):



BnBr (7.10 mL, 59.8 mmol) was added to a cooled (0 °C) and stirred mixture of diacetone-D-glucose (13.0 g, 49.9 mmol) and NaH (60% on mineral oil, 6.00 g, 150 mmol) in DMF (150 mL). After 18 h, TLC analysis showed complete conversion of starting material. Methanol was added to quench the excess NaH. The reaction mixture was diluted with water

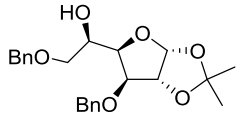
(250 mL) and extracted with Et_2O (3 x). The organic layers were combined and washed successively with sat. aq. $NaHCO_3$ and water, dried (Na_2SO_4), filtered and concentrated. The crude product was purified by silica gel column chromatography (4:1, PE:EtOAc) to give pure **10** (16.9 g, 48.2 mmol) in yield of 97% as light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.25 (m, 5H, H_{Ar} Bn), 5.90 (d, *J* = 3.7 Hz, 1H, H-1), 4.72 – 4.55 (m, 3H, 2 x CH*H* Bn, H-2), 4.37 (dt, *J* = 7.8, 6.0 Hz, 1H, H-5), 4.16 – 4.10 (m, 2H, H-6a, H-4), 4.05 – 3.97 (m, 2H, H-6b, H-3), 1.50 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 1.31 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.7 (C_q Bn), 128.5, 128.0, 127.8 (CH_{Ar} Bn), 111.7, 108.9 (2 x C_q isopropyl), 105.2 (C-1), 82.6 (C-2), 81.6 (C-3), 81.3 (C-4), 72.5 (C-5), 72.3 (CH_2 Bn), 67.4 (C-6), 27.0, 26.9, 26.4, 25.6 (4 x CH_3).

3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-*gluco*-furanoside (11):



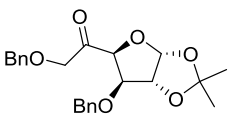
10 (14.0 g, 40.0 mmol) was dissolved in a mixture of acetic acid (45 mL) and water (20 mL), and the reaction mixture was stirred for 72 h at r.t. After TLC analysis showed complete consumption of starting material, ethyl acetate (100 mL) was added. The organic layer was washed successively with sat. aq. $NaHCO_3$, water and brine. The organic layer was dried (Na_2SO_4), filtrated and concentrated. The crude product was purified by silica gel column chromatography to gain **20** (9.92 g, 32.0 mmol) in 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.27 (m, 5H, H_{Ar} Bn), 5.91 (dd, *J* = 3.9, 1.5 Hz, 1H, H-1), 4.70 (dd, *J* = 11.8, 1.9 Hz, 1H, CH*H* Bn), 4.60 (dd, *J* = 3.9, 1.5 Hz, 1H, H-2), 4.56 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.13 – 4.06 (m, 2H, H-3, H-4), 4.02 (dd, *J* = 8.9, 4.8 Hz, 1H, H-5), 3.79 (d, *J* = 11.0 Hz, 1H, H-6a), 3.67 (dd, *J* = 11.6, 5.5 Hz, 1H, H-6b), 1.47 (s, 3H, CH_3), 1.30 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.3 (C_q Bn), 128.7, 128.2, 127.9 (CH_{Ar} Bn), 111.9 (C_q isopropyl), 105.2 (C-1), 82.2 (C-2), 82.0 (C-3), 80.0 (C-4), 72.2 (C-5), 69.2 (CH_2 Bn), 64.7 (C-6), 26.8, 26.3 (2 x CH_3).

3,6-Di-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*gluco*-furanoside (12):



To a solution of **11** (8.29 g, 26.7 mmol) in toluene (250 mL) was added dibutyl tin oxide (10.0 g, 40.0 mmol). The reaction mixture was heated to reflux and stirred for 8 hours under Dean-Stark conditions. TBABr (1.03 g, 4.04 mmol) and benzyl bromide (6.36 mL, 53.6 mmol) were added to the solution. The reaction mixture was refluxed for another 18 h. The solvent was evaporated, and the residue was purified by silica gel column chromatography (5:1 → 3:1, PE:EtOAc) to give **12** (9.61 g, 24.0 mmol, yield 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.27 (m, 10H, H_{Ar} Bn), 5.94 (d, *J* = 3.7 Hz, 1H, H-1), 4.68 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.59 – 4.47 (m, 3H, 3 x CH*H* Bn), 4.61 (d, *J* = 3.6 Hz, 1H, H-2), 4.21 – 4.15 (m, 2H, H-3, H-5), 4.11 (d, *J* = 1.9 Hz, 1H, H-4), 3.75 (d, *J* = 9.2 Hz, 1H, H-6a), 3.61 (d, *J* = 9.9 Hz, 1H, H-6b), 1.49 (s, 3H, CH_3), 1.32 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.0, 137.3 (C_q Bn), 128.6, 128.5, 128.1, 127.8 (CH_{Ar} Bn), 111.8 (C_q isopropyl), 105.1 (C-1), 82.3 (C-2), 82.1 (C-4), 79.8 (C-3), 73.5 (CH_2 Bn), 72.4 (CH_2 Bn), 72.1 (C-6), 68.1 (C-5), 26.8, 26.3 (2 x CH_3).

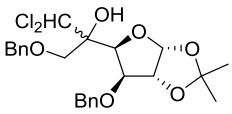
1,2-*O*-Isopropyl-3,6-di-*O*-benzyl-α-D-*xylo*-hexofuranoside-5-ulose (13):



12 (8.62 g, 21.5 mmol) dissolved in dry DCM (100 mL) was added to a suspension of pyridinium chlorochromate (PCC, 15.34 g, 71.1 mmol) and activated 4 Å molecular sieves in dry DCM (300 mL). The reaction mixture was stirred under argon atmosphere at 30 °C overnight. 2-Propanol was then added to quench the reaction. Diethyl ether (200 mL) was added to dilute the dark brown suspension and the mixture was filtered through a pad of Celite. The filtrate was concentrated, and the residue was purified by silica gel column chromatography and to give pure **13** (4.54 g, 11.40 mmol, yield 53%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.22 (m, 10H, H_{Ar} Bn), 6.05 (d, *J* = 3.6 Hz, 1H, H-1), 4.82 (d, *J* = 3.7 Hz, 1H, H-4), 4.62 (d, *J* = 3.6 Hz, 1H, H-2), 4.60 (d, *J* = 12.0, 1H, CH*H* Bn), 4.59 (d, *J* = 12.0 Hz, CH*H* Bn), 4.50 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.49 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.46 (d, *J* = 18.8 Hz, 1H, H-6a), 4.39 (d, *J* = 18.8 Hz, 1H, H-6b),

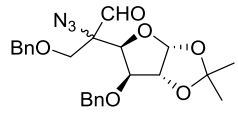
4.38 (d, *J* = 3.7 Hz, 1H, H-3), 1.49 (s, 3H, CH_3), 1.34 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.6 (C=O), 137.4, 136.7 (C_q Bn), 128.6, 128.5, 128.2, 127.9 (CH_{Ar} Bn), 112.5 (C_q isopropyl), 105.9 (C-1), 84.9 (C-4), 83.6 (C-3), 82.1 (C-2), 74.4 (C-6), 73.2, 72.6 (CH_2 Bn), 26.9, 26.3 (2 x CH_3).

1,2-*O*-Isopropyl-3,6-di-*O*-benzyl-5-*C*-dichloromethyl-α-D-*gluco*/β-L-*ido*-furanoside (14):



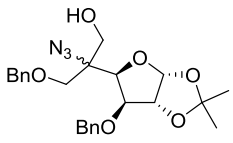
To a cooled (-78 °C) solution of LDA (36 mmol, 18 mL, 2 M in THF) in dry THF (45 mL) was added DCM (18 mL). After 30 minutes, **13** (4.48 g, 11.3 mmol) dissolved in DCM (18 mL) was added. After another 30 minutes temperature was allowed to rise to r.t. When TLC analysis indicated complete conversion of starting material, sat. aq. NH_4Cl was added. The mixture was extracted with EtOAc (100 mL) and the organic layer was washed successively with water and brine, dried (Na_2SO_4), filtered and concentrated. The residue was purified by silica gel column chromatography (20:1 → 10:1, pentane:EtOAc) to gain **14** (3.00 g, 6.21 mmol, yield 55%), as a mixture of two inseparable diastereo-isomers at a ratio of 3:2. NMR data of the major diastereoisomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.00 (m, 10H, H_{Ar} Bn), 6.11 (s, 1H, C*H*Cl_2), 5.89 (d, *J* = 3.9 Hz, 1H, H-1), 4.58 (d, *J* = 3.9 Hz, 1H, H-2), 4.56 – 4.43 (m, 5H, H-4, 2 x CH_2 Bn), 4.36 (d, *J* = 3.0 Hz, 1H, H-4), 3.94 (d, *J* = 10.0 Hz, 1H, H-6a), 3.85 (d, *J* = 10.0 Hz, 1H, H-6b), 1.41 (s, 3H, CH_3), 1.25 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.9, 135.9 (C_q Bn), 128.8 – 127.7 (CH_{Ar} Bn), 112.0 (C_q isopropyl), 103.7 (C-1), 84.9 (C-3), 81.5 (C-2), 79.7 (C-5), 75.8 (C-4), 73.8, 72.2 (CH_2 Bn), 72.2 (C-6), 26.7, 26.3 (2 x CH_3).

5-Deoxy-5-azido-5-*C*-benzyloxymethyl-3-*O*-benzyl-1,2-*O*-isopropyl-α-D-*gluco*/β-L-*ido*-furano-1,6-dialdose (15):



A mixture of **14** (2.69 g, 5.58 mmol), TBAI (1.07 g, 2.89 mmol) and NaN_3 (1.96 g, 30.0 mmol) in DMF (60 mL) was stirred at 115 °C for 18 h. After TLCMS analysis showed complete consumption of **14**, the reaction was quenched by the addition of water (100 mL) and extracted with EtOAc (75 mL x 3). The combined organic layers were washed with water (2 x) and brine (2 x), dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel column chromatography (10:1, pentane:EtOAc) to give **15** (1.74 g, 3.85 mmol, yield 69%). It is a mixture of two inseparable diastereo-isomers at a ratio of 3:2. NMR data of the major diastereoisomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.69 (s, 1H, C*H*O), 7.47 – 7.30 (m, 10H, H_{Ar} Bn), 5.93 (d, *J* = 3.6 Hz, 1H, H-1), 4.67 – 4.41 (m, 5H, H-4, 2 x CH_2 Bn), 4.28 (d, *J* = 3.0 Hz, 1H, H-4), 4.08 (d, *J* = 10.2 Hz, 1H, H-6a), 4.05 (d, *J* = 3.0 Hz, 1H, H-3), 3.86 (d, *J* = 10.2 Hz, 1H, H-6b), 1.48 (s, 3H, CH_3), 1.32 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.3 (C=O), 137.2, 136.3 (C_q Bn), 128.6, 128.6, 128.3, 127.9, 127.6 (CH_{Ar} Bn), 112.3 (C-5), 105.2 (C-1), 81.9 (C-2), 81.4 (C-4), 81.1 (C-3), 73.7, 72.8 (2 x CH_2 Bn), 70.3 (C-6), 26.8, 26.2 (2 x CH_3).

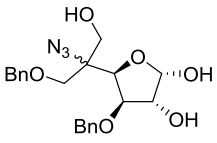
5-Deoxy-5-azido-5-*C*-benzyloxymethyl-3-*O*-benzyl-1,2-*O*-isopropyl-α-D-*gluco*/β-L-*ido*-furanoside (16):



$NaBH_4$ (0.33 g, 1.85 mmol) was added to a solution of **15** (1.68 g, 3.85 mmol) in methanol (10 mL) at 0 °C. The reaction mixture was stirred for 2 hours at 0 °C, and quenched by the addition of sat. aq. NH_4Cl. The volatiles were evaporated. The residue was extracted with EtOAc (3 x). The organic layer was washed with water and brine, dried (Na_2SO_4), filtered and concentrated. The crude product was purified by silica gel column chromatography (20:1 → 10:1, pentane:EtOAc) to give **16** (1.56 g, 3.43 mmol, yield 89%), as a mixture of two inseparable diastereo-isomers at a ratio of 3:2. NMR data of the major diastereoisomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.24 (m, 10H, H_{Ar} Bn), 5.91 (d, *J* = 3.8 Hz, 1H, H-1), 4.63 (d, *J* = 11.5 Hz, 1H, CH*H* Bn), 4.56 (d, *J* = 3.5 Hz, 1H, H-2), 4.52 (d, *J* = 12.0 Hz, 1H, CH*H* Bn), 4.47 (d, *J* = 12.4 Hz, 1H, CH*H* Bn), 4.30 (d, *J* = 3.2 Hz, 1H, CH*H* Bn), 4.02 (d, *J* = 3.2 Hz, 1H, H-3), 3.90 (d, *J* = 11.9 Hz, 1H, H-6a),

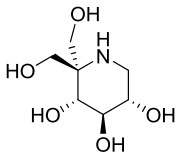
3.87 (d, *J* = 11.5 Hz, 1H, H-6b), 3.75 (d, *J* = 10.0 Hz, 1H, CH*H*OH), 3.67 (d, *J* = 10.1 Hz, 1H, CH*H*OH), 1.46 (s, 3H, CH_3), 1.30 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.6, 136.5 (C_q Bn), 128.6, 128.6, 128.5, 128.3, 127.9, 127.8, 127.7 (CH_{Ar} Bn), 112.0 (C_q isopropyl), 104.4 (C-1), 82.2 (C-4), 81.7 (C-2), 80.0 (C-3), 73.6, 72.1 (CH_2 Bn), 71.2 (CH_2OH), 66.0 (C-5), 63.6 (C-6), 26.8, 26.3 (2 x CH_3).

5-Deoxy-5-azido-5-*C*-benzyloxymethyl-3-*O*-benzyl-D-*gluco*/β-L-*ido*-furanoside (17):



16 (1.50 g, 3.29 mmol) was dissolved in a mixture of H_2O (15 mL) and TFA (15 mL) at 0 °C, the temperature was allowed to rise to r.t. and the mixture was stirred for 18 h. After TLC analysis indicated complete conversion of the starting material, TFA was removed by repetitive coevaporation with toluene. The reaction mixture was diluted with water (20 mL), extracted with EtOAc (90 mL) and washed with brine (2 x). The organic layer was dried (Na_2SO_4), filtered and concentrated. The crude product was purified by silica gel column chromatography to give **17** (0.93 g, 2.24 mmol, yield 68%). It is a mixture of two inseparable diastereo-isomers at a ratio of 3:2. NMR data of the major diastereoisomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.24 (m, 10H, H_{Ar} Bn), 5.47 (d, *J* = 4.6 Hz, 1H, H-1), 4.49 – 4.30 (m, 4H, 2 x CH_2 Bn), 4.21 (d, *J* = 2.8 Hz, 1H, H-3), 4.16 (dd, *J* = 4.0, 1.7 Hz, 1H, H-2), 3.99 (dd, *J* = 4.0, 1.6 Hz, 1H, H-4), 3.89 (d, *J* = 11.9 Hz, 1H, H-6a, 3.83 (d, *J* = 11.8 Hz, 1H, H-6b), 3.70 (d, *J* = 10.0 Hz, 1H, CH*H*OH), 3.67 (d, *J* = 10.2 Hz, 1H, CH*H*OH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.6, 137.0 (C_q Bn), 128.7, 128.5, 128.2, 127.9, 127.8, 127.8 (CH_{Ar} Bn), 103.2 (C-1), 84.2 (C-4), 77.2 (C-3), 74.1 (C-2), 72.5, 71.9 (2 x CH_2 Bn), 70.4 (CH_2OH), 66.4 (C-5), 63.6 (C-6).

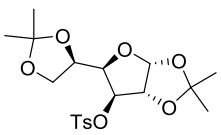
5-*C*-Hydroxymethyl-1-deoxynojirimycin (6):



Pd/C (10%, 0.28 g) was added to a solution of **17** (1.17 g, 2.82 mmol) in ethanol (50 mL) and pH of the solution was adjusted to 1 with 1M HCl. The reaction mixture was exposed to 5 bar of hydrogen and kept shaking for 24 hours. The reaction mixture was filtered over a pad of Celite and the filtrate was concentrated. The residue was purified by silica gel column chromatography (0% → 20% methanol in DCM + 1% NH_4OH) to gain **6** as light yellow oil (0.40 g, 2.09 mmol, yield 74%). ^{1}H NMR (400 MHz, MeOD) δ 3.86 (d, *J* = 12.1 Hz, 1H, H-6*a), 3.81 (d, *J* = 11.1 Hz, 1H, H-6a), 3.68 (d, *J* = 12.0 Hz, 1H, H-6*b), 3.67 (d, *J* = 11.1 Hz, 1H, H-6b), 3.64 (d, *J* = 9.6 Hz, 1H, H-4), 3.56 (dd, *J* = 9.2, 8.8 Hz, 1H, H-3), 3.58 – 3.51 (m, 1H, H-2), 3.07 (dd, *J* = 12.6, 4.6 Hz, 1H, H-1a), 2.86 – 2.78 (m, 1H, H-1b). ^{13}C NMR (100 MHz, MeOD) δ 74.7 (C-3), 71.3 (C-4), 70.1 (C-2), 62.0 (C-5), 61.8 (C-6), 57.3 (C-6*), 43.7 (C-1). $[\alpha]^{20}_D$ = -0.3 (c = 0.54, MeOH). IR/cm^{-1}: 3277, 2926, 1612, 1450, 1406, 1259, 1076, 1039, 933. HRMS: found 194.10222 $[C_7H_{15}NO_5+H]^+$, calculated for $[C_7H_{15}NO_5+H]^+$ 194.10230.

Synthesis of 5-*C*-Hydroxymethyl-1-deoxy-D-galactonojirimycin (7)

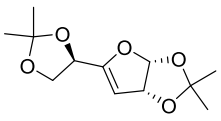
3-*O*-(*p*-Toluenesulfonyl)-1,2:5,6-di-*O*-isopropylidene-α-D-*gluco*-furanoside (18):



p-Toluenesulfonyl chloride (3.60 g, 1.88 mmol) was added to a solution of diacetone-D-glucose (2.50 g, 8.61 mmol) in pyridine (24 mL) and DCM (24 mL). The reaction mixture was stirred overnight at a temperature of 60 °C. The volatiles were removed, and the residue was dissolved in DCM (30 mL), and the organic layer was washed with sat. aq. $NaHCO_3$, dried (Na_2SO_4), filtered, concentrated and purified by silica gel column chromatography to give **18** (3.50 g, 8.44 mmol, yield 98%). R_F = 0.41 (5:3, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.3 Hz, 2H, H_{Ar} Ts), 7.34 (d, *J* = 8.1 Hz, 2H, H_{Ar} Ts), 5.92 (d, *J* = 3.6 Hz, 1H, H-1), 4.83 (d, *J* = 3.7 Hz, 1H, H-2), 4.80 (d, *J* = 2.3 Hz, 1H, H-3), 4.07 – 3.96 (m, 3H, H-4, H-5, H-6a), 3.91 (dd, *J* = 8.2, 3.9 Hz, 1H, H-6b), 2.46 (s, 3H, CH_3 Ts), 1.48 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.20 (s, 3H, CH_3), 1.15 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.1, 132.7, 130.2, 129.7, 128.4, 128.0 (C_{Ar} Ts), 112.5

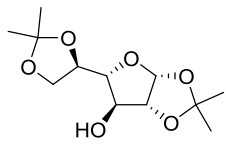
(C_q isopropyl), 109.1 (C_q isopropyl), 105.1 (C-1), 83.3 (C-2), 82.1 (C-3), 79.9 (C-4), 71.8 (C-5), 67.1 (C-6), 26.6, 26.2, 24.9, 21.7 (4 x CH_3), 14.2 (CH_3 Ts).

1,2:5,6-Di-*O*-isopropylidene-3-α-D-glucal (19):



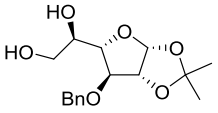
Potassium tert-butoxide (6.30 g, 10.1 mmol) was added to a solution of **18** (2.73 g, 6.59 mmol) in dried THF (40 mL) at 0 °C, and the mixture was stirred at 0 °C under argon atmosphere for 5 hours. Water (100 mL) was added and the reaction mixture was extracted with DCM (2 x 50 mL). The combined organic layers were washed successively with water and brine, dried (Na_2SO_4), filtered, concentrated and the residue was purified by silica gel column chromatography (5:1, PE:EtOAc) to give **19** (1.45 g, 5.99 mmol, yield 91%). R_F = 0.78 (5:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.09 (d, *J* = 5.2 Hz, 1H, H-1), 5.31 (ddd, *J* = 5.3, 2.3, 1.5 Hz, 1H, H-2), 5.26 (dd, *J* = 2.4, 1.2 Hz, 1H, H-3), 4.60 (dd, *J* = 7.0, 5.6 Hz, 1H, H-5), 4.17 (d, *J* = 8.4 Hz, 1H, H-6a), 3.99 (d, *J* = 8.5 Hz, 1H, H-6b), 1.48 (s, 6H, 2 x CH_3), 1.45 (s, 3H, CH_3), 1.40 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0 (C-4), 112.3 (C_q isopropyl), 110.3 (C_q isopropyl), 106.6 (C-1), 99.0 (C-3), 83.4 (C-2), 71.3 (C-5), 67.0 (C-6), 28.2, 27.9, 26.2, 25.5 (4 x CH_3).

1,2:5,6-Di-*O*-isopropylidene-α-D-*galacto*-furanoside (20):



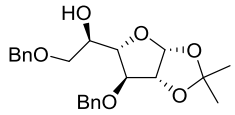
To a solution of **19** (0.49 g, 2.02 mmol) in THF (3 mL) was added BH_3·THF complex (1M, 2.5 mL, 2.5 mmol) at 0 °C under argon atmosphere. After 4 hours a mixture of aq. NaOH (2M, 0.9 mL) and 30% H_2O_2 (0.4 mL) was added to the reaction mixture. The reaction was stirred at r.t. for 1 hour, and the volatiles were evaporated. The residue was diluted with water (5 mL), and the water layer extracted with EtOAc (4 x 50 mL). The combined organic layers were dried (Na_2SO_4), filtered and evaporated. The crude product was crystallized from EtOAc and pentane to give **20** as a crystalline product (0.40 g, 1.53 mmol, 75%). R_F = 0.24 (5:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.88 (d, *J* = 3.9 Hz, 1H, H-1), 4.55 (dd, *J* = 3.9, 1.4 Hz, 1H, H-2), 4.37 (q, *J* = 6.8 Hz, 1H, H-5), 4.13 (dd, *J* = 4.5, 1.3 Hz, 1H, H-3), 4.08 (dd, *J* = 8.4, 6.6 Hz, 1H, H-6a), 3.88 (d, *J* = 6.8 Hz, 1H, H-4), 3.86 (dd, *J* = 8.0, 7.0 Hz, 1H, H-6b), 1.55 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 1.36 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 113.8, 110.0 (2 x C_q isopropyl), 105.1 (C-1), 87.7 (C-2), 86.0 (C-4), 76.3 (C-3), 75.5 (C-4), 65.8 (C-6), 27.6, 26.9, 26.7, 25.4 (4 x CH_3).

3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-*galacto*-furanoside (22):



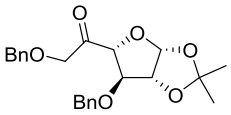
To a solution of **20** (4.00 g, 15.4 mmol) in DMF (150 mL) at 0 °C under argon atmosphere, was added NaH (60% mineral oil, 1.85 g, 46.3 mmol). After 30 minutes, BnBr (40 mL, 33.7 mmol) was added. The reaction mixture was stirred at r.t. overnight. The excess NaH was quenched by the addition of methanol, and the volatiles were evaporated. The residue was dissolved in DCM, washed with water and brine, dried (Na_2SO_4), filtered and concentrated. The crude product **21** (R_F = 0.18, 5:3, PE:EtOAc) was dissolved in water (10 mL) and AcOH (60 mL). The reaction mixture was stirred at r.t. overnight. The volatiles were evaporated, and the residue was purified by silica gel column chromatography (3:2 → 1:1, PE:EtOAc) to give **22** (4.12 g, 13.2 mmol, 86% yield over the 2 steps). R_F = 0.82 (5:3, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.30 (m, 5H, H_{Ar} Bn), 5.92 (d, *J* = 4.1 Hz, 1H, H-1), 4.69 (dd, *J* = 4.1, 1.1 Hz, 1H, H-2), 4.65 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.57 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.14 (dd, *J* = 6.7, 3.5 Hz, 1H, H-4), 4.01 (dd, *J* = 3.5, 1.1 Hz, 1H, H-3), 3.80 (ddd, *J* = 6.7, 4.8, 3.8 Hz, 1H, H-5), 3.70 (dd, *J* = 11.8, 3.8 Hz, 1H, H-6a), 3.59 (dd, *J* = 11.7, 4.8 Hz, 1H, H-6b), 1.53 (s, 3H, CH_3), 1.35 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.1 (C_q Bn), 128.7, 128.3, 128.0 (CH_{Ar} Bn), 113.3 (C_q isopropyl), 105.7 (C-1), 85.4 (C-2), 85.4 (C-4), 83.1 (C-3), 72.0 (CH_2 Bn), 70.9 (C-5), 63.9 (C-6), 27.2, 26.5 (2 x CH_3).

3,6-Di-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-*galacto*-furanoside (23):



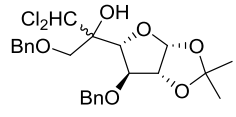
23 was synthesized from **22** (3.30 g, 10.6 mmol) in a yield of 82% (3.49 g, 8.72 mmol), as a thick yellow oil, as described for the synthesis of **12**. R_F = 0.80 (9:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.30 (m, 10H, H_{Ar} Bn), 5.95 (d, *J* = 4.2 Hz, 1H, H-1), 4.71 (d, *J* = 3.9 Hz, 1H, H-2), 4.61 (d, *J* = 11.4 Hz, 1H, CH*H* Bn), 4.57 (s, 2H, CH_2 Bn), 4.54 (d, *J* = 11.7 Hz, 1H, CH*H* Bn)), 4.19 (dd, *J* = 6.5, 3.4 Hz, 1H, H-4), 4.12 (dd, *J* = 3.4, 1.1 Hz, 1H, H-3), 3.98 (q, *J* = 5.8 Hz, 1H, H-5), 3.59 (dd, *J* = 9.9, 5.7 Hz, 1H, H-6a), 3.55 (dd, *J* = 9.9, 5.3 Hz, 1H, H-6b), 1.57 (s, 3H, CH_3), 1.38 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.9, 137.2 (C_q Bn), 128.6, 128.5, 128.4, 128.1, 128.0, 127.8, 127.8, 127.8 (CH_{Ar} Bn), 113.0 (C_q isopropyl), 105.5 (C-1), 85.6 (C-2), 85.2 (C-4), 83.1 (C-3), 73.6 (CH_2 Bn), 71.9 (CH_2 Bn), 71.4 (C-6), 69.7 (C-5), 27.1, 26.4 (2 x CH_3).

3,6-Di-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-*arabino*-hexofuranoside-5-ulose (24):



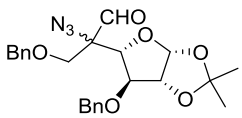
24 was synthesized from **23** (3.50 g, 8.74 mmol) in a yield of 92% (3.20 g, 8.04 mmol), as a thick yellow oil, as described for the synthesis of **13**. R_F = 0.67 (10:3, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 10H, H_{Ar} Bn), 5.98 (d, *J* = 3.8 Hz, 1H, H-1), 4.70 (d, *J* = 18.4 Hz, 1H, CH*H* Bn), 4.65 – 4.61 (m, 3H, H-2, H-3, CH*H* Bn), 4.60 – 4.56 (m, 3H, H_2-6, CH*H* Bn), 4.52 (d, *J* = 1.0 Hz, 1H, H-4), 4.37 (d, *J* = 18.4 Hz, 1H, CH*H* Bn), 1.31 (s, 3H, CH_3), 1.25 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.0 (C-5), 137.2 – 127.8 (C_{Ar} Bn), 112.3 (C_q isopropyl), 106.5 (C-1), 88.6 (C-2), 83.6 (C-4), 83.5 (C-3), 73.4 (CH_2 Bn), 73.1 (CH_2 Bn), 72.0 (C-6), 25.7, 25.6 (2 x CH_3).

1,2-*O*-Isopropyl-3,6-di-*O*-benzyl-5-*C*-dichloroemethyl-α-D-*galacto*/β-L-*altro*-furanoside (25):



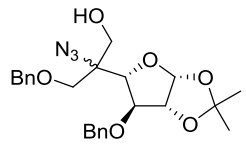
25 was synthesized from **24** (3.20 g, 8.03 mmol) in a yield of 74% (2.87 g, 5.94 mmol) as a thick yellow oil as described for the synthesis of **14**. R_F = 0.52 (9:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.24 (m, 10H, H_{Ar} Bn), 5.95 – 5.93 (m, 1H, $CHCl_2$), 5.80 (dd, *J* = 3.9, 1.6 Hz, 1H, H-1), 4.66 (d, *J* = 11.6, 1H, CH*H* Bn), 4.63 (dd, *J* = 3.8, 1.4 Hz, 1H, H-2), 4.60 (d, *J* = 11.6, 1H, CH*H* Bn), 4.56 (d, *J* = 1.7 Hz, 2H, CH_2 Bn), 4.50 – 4.46 (m, 1H, H-3), 4.44 – 4.38 (m, 1H, H-4), 3.81 (m, 2H, H_2-6), 1.51 (s, 3H, CH_3), 1.35 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.5 – 127.8 (C_{Ar} Bn), 114.1 (C_q isopropyl), 104.8 (C-1), 85.2 (C-2), 84.8 (C-4), 81.7 (C-3), 76.6 (C-5), 75.7 ($CHCl_2$), 73.8 (CH_2 Bn), 72.3 (CH_2 Bn), 70.1 (C-6), 27.2, 26.7 (2 x CH_3). HRMS: found 505.11521 $[C_{24}H_{28}Cl_2O_6+Na]^+$, calculated for $[C_{24}H_{28}Cl_2O_6+Na]^+$ 505.11552.

5-Deoxy-5-azido-5-*C*-benzyloxymethyl-3-*O*-benzyl-1,2-*O*-isopropyl-α-D-*galacto*/β-L-*altro*-furano-1,6-dialdose (26):



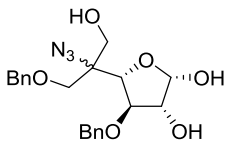
26 was synthesized from **25** (2.90 g, 6.00 mmol) in a yield of 93% as a thick yellow oil as described for the synthesis of **15**. R_F = 0.52 (9:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.70 (s, 1H, CHO), 7.54 – 7.19 (m, 10H, H_{Ar} Bn), 5.75 (d, *J* = 4.0 Hz, 1H, H-1), 4.69 (d, *J* = 11.3 Hz, 1H, CH*H* Bn), 4.64 (dd, *J* = 4.0, 1.5 Hz, 1H, H-2), 4.54 (d, *J* = 11.3 Hz, 1H, CH*H* Bn), 4.52 (d, *J* = 4.1 Hz, 2H, CH_2 Bn), 4.14 (dd, *J* = 6.3, 1.5 Hz, 1H, H-3), 4.11 (d, *J* = 6.3 Hz, 1H, H-4), 3.96 (d, *J* = 10.0 Hz, 1H, H-6a), 3.60 (d, *J* = 10.0 Hz, 1H, H-6b), 1.61 (s, 3H, CH_3), 1.40 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.8 (CHO), 136.9, 136.7 (C_q Bn), 128.5, 128.2, 128.1, 128.0, 127.7 (CH_{Ar} Bn), 115.1 (C_q isopropyl), 104.6 (C-1), 85.4 (C-2), 82.0 (C-3), 81.9 (C-4), 73.8 (CH_2 Bn), 72.4 (CH_2 Bn), 70.8 (C-5), 70.5 (C-6), 27.5, 27.1 (2 x CH_3). HRMS: found 476.17913 $[C_{24}H_{27}N_3O_6+Na]^+$, calculated for $[C_{24}H_{27}N_3O_6+Na]^+$ 476.19721.

5-Deoxy-5-azido-5-*C*-benzyloxymethyl-3-*O*-benzyl-1,2-*O*-isopropyl-α-D-*galacto*/β-L-*altro*-furanoside (27):



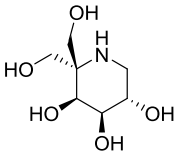
27 was synthesized from **26** (2.50 g, 5.51 mmol) in a yield of 82% (2.06 g, 4.52 mmol), as thick yellow oil, as described for the synthesis of **16**. R_F = 0.22 (9:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.18 (m, 10H, H_{Ar} Bn), 5.76 (d, *J* = 4.0 Hz, 1H, H-1), 4.67 (d, *J* = 11.3 Hz, 1H, CH*H* Bn), 4.62 (dd, *J* = 4.1, 1.5 Hz, 1H, H-2), 4.50 (d, *J* = 12.0, 1H, CH*H* Bn), 4.49 (s, 2H, CH_2OH), 4.22 (dd, *J* = 6.4, 1.5 Hz, 1H, H-3), 3.99 (d, *J* = 12.0 Hz, 1H, H-6a), 3.95 (d, *J* = 6.4 Hz, 1H, H-4), 3.93 (d, *J* = 11.9 Hz, 1H, H-6b), 4.04 – 3.86 (m, 3H, H-4, H_2-6), 3.61 (d, *J* = 9.9 Hz, 1H, CH*H* Bn), 3.52 (d, *J* = 10.0 Hz, 1H, CH*H* Bn), 1.60 (s, 3H, CH_3), 1.39 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.7 – 127.9 (C_{Ar} Bn), 115.2 (C_q isopropyl), 104.7 (C-1), 86.1 (C-2), 83.4 (C-4), 82.4 (C-3), 74.0 (CH_2OH), 72.7 (CH_2 Bn), 71.4 (CH_2 Bn), 66.1 (C-5), 63.9 (C-6), 27.8, 27.4 (2 x CH_3). HRMS: found 478.19451 $[C_{24}H_{29}N_3O_6+Na]^+$, calculated for $[C_{24}H_{29}N_3O_6+Na]^+$ 478.19486.

5-Deoxy-5-azido-5-*C*-benzyloxymethyl-3-*O*-benzyl-α-D-*galacto*/β-L-*altro*-furanoside (28):



28 was synthesized from **27** (2.08 g, 4.57 mmol) in a yield of 63% (1.31 g, 2.88 mmol), as a thick yellow oil, as described for the synthesis of **17**. **28** was obtained as an inseparable mixture of diastereo isomers (ratio 1:0.9). NMR data of the major diastereoisomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.20 (d, *J* = 3.9 Hz, 1H, H-1), 4.61 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.45 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.43 (s, 2H, C*H*$_2$OH), 4.07 (d, *J* = 3.8 Hz, 1H, H-3), 4.03 (t, *J* = 4.0 Hz, 1H, H-2), 3.93 (dd, *J* = 11.8, 4.7 Hz, 1H, H-6a), 3.89 (d, *J* = 5.3 Hz, 1H, H-4), 3.85 (d, *J* = 11.8 Hz, 1H, H-6b), 3.59 (d, *J* = 10.1 Hz, 1H, CH*H* Bn), 3.42 (d, *J* = 10.0 Hz, 1H, CH*H* Bn). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.6, 137.4 (C_q Bn), 128.7, 128.7, 128.4, 128.4, 128.2, 128.2, 127.8, 127.8 (CH_{Ar} Bn), 97.1 (C-1), 84.0 (C-3), 81.3 (C-4), 76.0 (C-2), 73.9 (CH_2OH), 72.1 (CH_2 Bn), 71.1 (CH_2 Bn), 66.5 (C-5), 62.4 (C-6). HRMS: found 438.16347 $[M+Na]^+$, calculated for $[+Na]^+$ 438.19486.

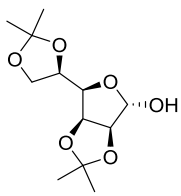
5-*C*-Hydroxymethyl-1-deoxy-D-galactonojirimycin (7):



7 was synthesized from **28** (1.00 g, 2.42 mmol) in a yield of 91% (0.42 g, 2.20 mmol), as thick yellow oil, as described for the synthesis of **6**. R_F = 0.26 (1% NH_4OH in MeOH). ^{1}H NMR (400 MHz, MeOD) δ 3.99 (d, *J* = 3.3 Hz, 1H, H-4), 3.87 (d, *J* = 11.3 Hz, 1H, H-6a), 3.83 (td, *J* = 7.8, 4.3 Hz, 1H, H-2), 3.75 (d, *J* = 11.4 Hz, 1H, H-6*a), 3.71 (dd, *J* = 7.6, 3.3 Hz, 1H, H-3), 3.68 (d, *J* = 11.2 Hz, 1H, H-6b), 3.63 (d, *J* = 11.3 Hz, 1H, H-6*b), 3.13 (dd, *J* = 13.2, 4.3 Hz, 1H, H-1a), 2.71 (dd, *J* = 13.2, 7.9 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, MeOD) δ 72.0 (C-3), 68.4 (C-4), 68.3 (C-2), 61.9 (C-6), 60.9 (C-5), 59.7 (C-6*), 43.6 (C-1). $[\alpha]^{20}_D$ = +0.8 (c = 0.57, MeOH). IR/cm^{-1}: 3275, 2922, 2497, 1608, 1049, 1338, 1247, 1114, 1056, 1024. HRMS: found $[C_7H_{15}NO_5+H]^+$ 194.10221, calculated for $[C_7H_{15}NO_5+H]^+$ 194.10230.

Synthesis of 5-*C*-hydroxymethyl-1-deoxy-D-mannonojirimycin (8)

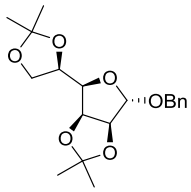
2,3:5,6-Di-*O*-isopropyl-α-D-*manno*-furanoside (29):



To a solution of D-mannose (36.0 g, 180 mmol) in dry acetone (1000 mL) at r.t. was added tetrabutylammonium tribromide (TBATB, 1.97 g, 4.08 mmol).[6] The reaction was monitored by TLC analysis. After complete conversion of the starting material, acetone was removed on a rotary evaporator. Title compound **29** was isolated by crystallization (3:1, pentane:EtOAc, 30.2 g, 116 mmol, yield 64%). R_F = 0.40 (10:3, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.36 (d, *J* = 2.7 Hz, 1H, H-1), 4.80 (dd, *J* = 5.9, 3.7 Hz, 1H, H-3), 4.60 (d, *J* = 5.9 Hz, 1H, H-2), 4.40 (q, *J* = 4.0 Hz, 1H, H-5), 4.16 (dd, *J* = 7.2, 3.6 Hz, 1H, H-4), 4.07 (d, *J* = 5.9 Hz, 2H, H-6a, H-6b), 1.46 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 1.33 (s, 3H, CH_3). ^{13}C NMR

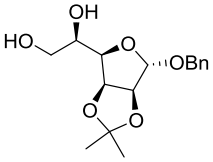
(100 MHz, $CDCl_3$) δ 112.3, 108.9 (2 x C_q isopropyl), 100.8 (C-1), 85.3 (C-2), 79.7 (C-4), 79.4 (C-3), 73.1 (C-5), 66.2 (C-6), 26.5, 25.6, 24.9, 24.2 (4 x CH_3).

Benzyl-2,3:5,6-di-*O*-isopropyl-α-D-*manno*-furanoside (30):



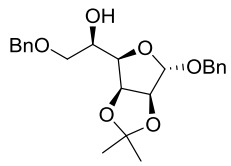
To a solution of **29** (1.28 g, 4.92 mmol) in THF (10 mL) was successively added freshly powdered potassium hydroxide (0.48 g, 8.56 mmol), 18-crown-6 (0.055 g, 0.21 mmol) and benzyl bromide (0.67 mL, 0.96 g, 5.64 mmol). The mixture was stirred at r.t. and the reaction was monitored by TLC analysis. After complete conversion of the starting material, the mixture was diluted with DCM and washed with water (3 x). The organic layer was dried (Na_2SO_4), filtered and concentrated, and the residue was purified by silica gel column chromatography (9:1, PE:EtOAc) to gain **30** (1.29 g, 3.68 mmol, yield 75%), R_F = 0. 70 (6:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.27 (m, 5H, H_{Ar} Bn), 5.08 (s, 1H, H-1), 4.80 (dd, *J* = 5.9, 3.6 Hz, 1H, H-3), 4.67 (d, *J* = 5.9 Hz, 1H, H-2), 4.64 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.49 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.11 (ddd, *J* = 7.9, 6.3, 4.3 Hz, 1H, H-5), 4.14 (dd, *J* = 8.7, 6.3 Hz, 1H, H-6a), 4.02 (dd, *J* = 8.8, 4.4 Hz, 1H, H-6b), 4.00 (dd, *J* = 8.0, 3.6 Hz, 1H, H-4), 1.46 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 1.32 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.4 (C_q Bn), 128.6 – 127.9 (CH_{Ar} Bn), 112.7, 109.4 (2 x C_q isopropyl), 105.7 (C-1), 85.2 (C-2), 80.5 (C-4), 79.7 (C-3), 73.2 (C-5), 69.3 (CH_2 Bn), 67.1 (C-6), 27.1, 26.0, 25.3, 24.6 (4 x CH_3).

Benzyl-2,3-*O*-isopropyl-α-D-*manno*-furanoside (31):



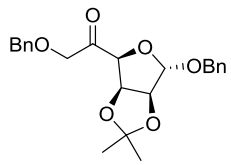
31 was synthesized from **30** (15.00 g, 42.84 mmol) in a yield of 81% (10.8 g, 34.8 mmol) as described for the synthesis of **11**. R_F = 0.19 (5:3, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.26 (m, 5H, H_{Ar} Bn), 5.10 (s, 1H, H-1), 4.85 (dd, *J* = 5.9, 3.6 Hz, 1H, H-3), 4.65 (d, *J* = 6.0 Hz, 1H, H-2), 4.62 (d, *J* = 11.9 Hz, 1H, CH*H* Bn), 4.48 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.05 – 3.98 (m, 1H, H-5), 3.95 (dd, *J* = 8.3, 3.6 Hz, 1H, H-4), 3.82 (dd, *J* = 11.5, 3.2 Hz, 1H, H-6a), 3.65 (dd, *J* = 11.5, 5.9 Hz, 1H, H-6b), 3.28 (s, 1H, OH), 2.96 (s, 1H, OH), 1.46 (s, 3H, CH_3), 1.32 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.2 (C_q Bn), 128.4, 128.0, 127.8 (CH_{Ar} Bn), 112.6 (C_q isopropyl), 105.3 (C-1), 84.7 (C-2), 80.0 (C-3), 79.2 (C-4), 70.1 (C-5), 69.1 (CH_2 Bn), 64.3 (C-6), 28.8, 24.5 (2 x CH_3).

Benzyl-2,3-*O*-isopropyl-6-*O*-benzyl-α-D-*manno*-furanoside (32):



32 was synthesized from **31** (10.7 g, 34.4 mmol) in a yield of 76% (10.5 g, 26.2 mmol) as thick yellow oil, as described for the synthesis of **12**. R_F = 0.64 (5:3, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 10H, 2 x H_{Ar} Bn), 5.09 (s, 1H, H-1), 4.87 (dd, *J* = 5.9, 3.7 Hz, 1H, H-3), 4.65 (d, *J* = 5.9 Hz, 1H, H-2), 4.64 (d, *J* = 11.9 Hz, 1H, CH*H* Bn), 4.62 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.58 (d, *J*= 11.9 Hz 1H, CH*H* Bn), 4.44 (d, *J*= 11.7 Hz 1H, CH*H* Bn), 4.15 (ddd, *J* = 8.4, 5.8, 3.3 Hz, 1H, H-5), 4.03 (dd, *J* = 8.3, 3.6 Hz, 1H, H-4), 3.73 (dd, *J* = 9.8, 3.3 Hz, 1H, H-6a), 3.63 (dd, *J* = 9.8, 5.7 Hz, 1H, H-6b), 1.47 (s, 3H, CH_3), 1.33 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.1, 137.4 (2 x C_q Bn), 128.6 – 127.8 (CH_{Ar} Bn), 112.7 (C_q isopropyl), 105.4 (C-1), 85.0 (C-2), 80.2 (C-3), 79.1 (C-4), 73.6 (CH_2 Bn), 71.9 (C-6), 69.1 (CH_2 Bn), 69.0(C-5), 26.1, 24.7(2 x CH_3).

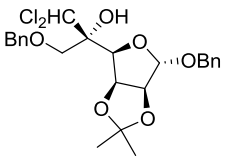
Benzyl-2,3-*O*-isopropyl-6-*O*-benzyl-α-D-lyxo-hexofuranoside-5-ulose (33):



33 (4.21 g, 10.5 mmol) was synthesized from **32** in a yield of 88% (3.66 g, 9.18 mmol), as described for the synthesis of **13**. R_F = 0.63 (3:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.17 (m, 10H, H_{Ar} Bn), 5.23 (s, 1H, H-1), 5.11 (dd, *J* = 5.8, 4.2 Hz, 1H, H-3), 4.73 (d, *J* = 4.2 Hz, 1H, H-4), 4.67 (d, *J* = 11.6 Hz, CH*H* Bn), 4.65 (d, *J* = 11.6 Hz, CH*H* Bn), 4.64 (d, *J* = 5.8 Hz, 1H, H-2), 4.61 (d, *J* = 11.6 Hz, CH*H* Bn), 4.49 (d, *J* = 11.6 Hz, CH*H* Bn),

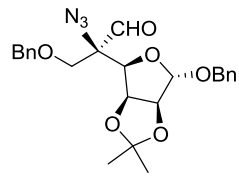
4.35 (s, 2H, H_2-6), 1.35 (s, 3H, CH_3), 1.26 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.0 (C=O), 137.2, 136.8 (2 x C_q Bn), 128.6 – 128.0 (CH_{Ar} Bn), 113.0 (C_q isopropyl), 105.4 (C-1), 84.3 (C-2), 84.2 (C-4), 80.7 (C-3), 74.1, 73.4 (2 x CH_2 Bn), 69.3 (C-6), 25.7, 24.5 (2 x CH_3).

Benzyl-2,3-*O*-isopropyl-6-*O*-benzyl-5-*C*-dichloromethyl-β-L-*gulo*-furanoside (34):



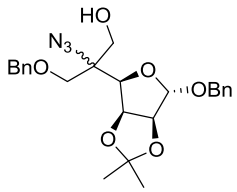
34 was synthesized from **33** in a yield of 66% (3.90 g, 8.34 mmol) as described for the synthesis of **14**. R_F = 0.53 (9:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.15 (m, 10H, H_{Ar} Bn), 6.19 (s, 1H, C*H*Cl_2), 5.17 (s, 1H, H-1), 5.05 (dd, *J* = 5.9, 3.4 Hz, 1H, H-3), 4.87 (s, 1H, -OH), 4.71 – 4.57 (m, 4H, H-4, 3 x CH*H* Bn), 4.39 (d, *J* = 11.4 Hz, 1H, CH*H* Bn), 4.28 (d, *J* = 3.4 Hz, 1H, H-2), 3.76 (d, *J* = 9.8 Hz, 1H, H-6a), 3.61 (d, *J* = 9.8 Hz, 1H, H-6b), 1.51 (s, 3H, CH_3), 1.34 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.0 – 127.8 (C_{Ar} Bn), 113.3 (C_q isopropyl), 105.0 (C-1), 85.0 (C-4), 81.7 (C-3), 77.9 (C-2), 73.9 (CH_2 Bn), 73.3 ($CHCl_2$), 70.8 (C-5), 69.1 (C-6), 25.8, 24.2 (2 x CH_3).

Benzyl-5-deoxy-5-azido-5-*C*-benzyloxymethyl-2,3-*O*-isopropylidene-α-D-*manno*-furano-1,6-dialdose (35):



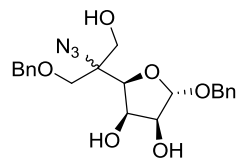
35 was synthesized from **34** (2.82 g, 5.84 mmol) in a yield of 87% (2.30 g, 5.07 mmol), as described for the synthesis of **15**. R_F = 0.52 (9:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1H, CHO), 7.39 – 7.28 (m, 10H, H_{Ar} Bn), 5.18 (s, 1H, H-1), 4.84 (dd, *J* = 5.9, 3.4 Hz, 1H, H-3), 4.70 – 4.60 (m, 4H, H-4, 3 x CH*H* Bn), 4.51 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.29 (d, *J* = 3.4 Hz, 1H, H-2), 3.90 (d, *J* = 10.2 Hz, 1H, H-6a), 3.82 (d, *J* = 10.2 Hz, 1H, H-6b), 1.45 (s, 3H, CH_3), 1.32 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.8 (CHO), 137.2 (C_q Bn), 128.6 – 127.7 (CH_{Ar} Bn), 113.3 (C_q isopropyl), 105.6 (C-1), 84.6 (C-4), 80.4 (C-2), 79.2 (C-3), 73.9 (CH_2 Bn), 70.5 ($C_q CN_3$), 69.9 (C-6), 69.5 (CH_2 Bn), 25.3, 24.2 (2 x CH_3).

Benzyl-5-deoxy-5-azido-5-*C*-benzyloxymethyl-2,3-*O*-isopropyl-α-D-*manno*/β-L-*gulo*-furanoside (36):



36 was synthesized from **35** (0.37 g, 0.82 mmol) in a yield of 80% (0.30 g, 0.65 mmol) as two inseparable diastereomers as described for the synthesis of **16**. R_F = 0.22 (9:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.27 (m, 10H, CH_{Ar} Bn), 5.09 (s, 1H, H-1), 4.77 (dd, *J* = 5.8, 3.3 Hz, 1H, H-3), 4.64 (d, *J* = 11.9 Hz, 1H, CH*H* Bn), 4.63 (d, *J* = 5.8 Hz, H-4), 4.62 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.55 (d, *J* = 11.9 Hz, 1H, CH*H* Bn), 4.45 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.23 (d, *J* = 3.2 Hz, 1H, H-2), 3.91 (d, *J* = 2.1 Hz, 2H, C*H*$_2$OH), 3.87 (d, *J* = 10.1 Hz, 1H, H-6a), 3.78 (d, *J* = 10.1 Hz, 1H, H-6b), 1.45 (s, 3H, CH_3), 1.29 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.5, 137.4 (C_q Bn), 128.5 – 127.7 (CH_{Ar} Bn), 112.9 (C_q isopropyl), 104.8 (C-1), 85.1(C-4), 79.8 (C-2), 79. 5 (C-3), 73.8 (CH_2 Bn), 70.9 (C-6), 69.3 (CH_2 Bn), 66.6 ($C_q N_3$), 63.7 (CH_2OH), 25.7, 24.3 (2 x CH_3).

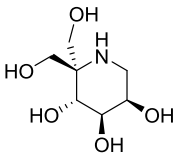
Benzyl-5-deoxy-5-azido-5-*C*-benzyloxymethyl-α-D-manno/β-L-*gulo*-furanoside (37):



36 (0.19 g, 0.43 mmol) was dissolved in a mixture of H_2O (0.6 mL) and TFA (1.8 mL) at 0 °C, the temperature was allowed to rise to r.t. and the mixture was stirred for 18 h. After TLC analysis indicated complete conversion of the starting material, the reaction mixture was diluted with water (5 mL), extracted with EtOAc (20 mL) and washed with brine (2 x). The organic layer was dried (Na_2SO_4), filtered and concentrated. The crude product was purified by silica gel column chromatography to give **37** (0.08 g, 0.19 mmol, yield 45%). R_F = 0.16 (5:3, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.27 (m, 10H, CH_{Ar} Bn), 5.09 (d, *J* = 2.2 Hz, 1H, H-1), 4.66 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.60 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.57 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.55 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.33 (ddd, *J* = 5.1,

4.1, 1.0 Hz, 1H, H-3), 4.14 (dd, *J* = 2.3, 5.3 Hz, 1H, H-2), 4.13 (dd, *J* = 4.0, 0.8 Hz, 1H, H-4), 3.94 (d, *J* = 11.6 Hz, 1H, H-6a), 3.84 (dd, *J* = 11.7, 0.8 Hz, 1H, H-6b), 3.75 (s, 2H, C*H*$_2$OH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.6, 136.8 (C_q Bn), 128.7 – 127.8 (CH_{Ar} Bn), 107.2 (C-1), 79.7 (C-4), 77.1 (C-2), 74.0 (CH_2 Bn), 71.6 (C-3), 70.4 (CH_2 Bn), 70.2 (CH_2OH), 66.8 (C-5), 63.8 (C-6).

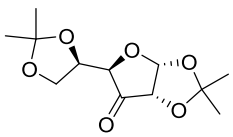
5-*C*-Hydroxymethyl-1-deoxy-D-mannonojirimycin (8):



8 was synthesized from **37** (0.83 g, 2.0 mmol) in a yield of 82% (0.32 g, 1.64 mmol) as described for the synthesis of **6**. ^{1}H NMR (400 MHz, MeOD) δ 4.17 (ddd, *J* = 1.5, 3.0, 3.7 Hz, 1H, H-2), 4.10 (d, *J* = 9.2 Hz, 1H, H-4), 3.95 (d, *J* = 11.6 Hz, 1H, H-6a), 3.94 (d, *J* = 12.6 Hz, 1H, H-6a'), 3.86 (dd, *J* = 9.2, 3.0 Hz, 1H, H-3), 3.77 (d, *J* = 11.6 Hz, 1H, H-6b), 3.71 (d, *J* = 12.5 Hz, 1H, H-6b'), 3.40 (dd, *J* = 1.5, 13.2 Hz, 1H, H-1a), 3.28 (dd, *J* = 3.7, 13.1 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, MeOD) δ 71.9 (C-3), 68.5 (C-4), 67.8 (C-2), 67.0 (C-5), 61.6 (C-6), 58.5 (C-6'), 45.7 (C-1). IR/cm^{-1}: 3307, 1636, 1451, 1229, 1073. HRMS: found 194.10223 $[C_7H_{15}NO_5+H]^+$, calculated for $[C_7H_{15}NO_5+H]^+$ 194.10230.

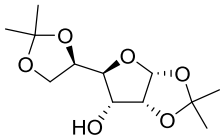
Synthesis of 5-*C*-hydroxymethyl-1-deoxy-D-allonojirimycin (9)

1,2:5,6-Di-*O*-isopropylidene-α-D-*allo*-furanoside-3-ulose (38):



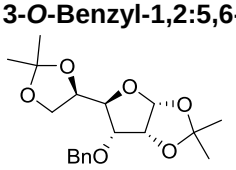
To a mixture of diacetone-D-glucose (15.0 g, 57.7 mmol) in anhydrous DCM (350 mL) and activated 4Å molecular sieves at 0 °C, was added pyridinium chlorochromate (PCC, 24.3 g, 112 mmol). The reaction mixture was stirred at r.t. overnight under argon atmosphere. The dark brown mixture was then filtered through a pad of silica gel, and the silica gel pad was rinsed with EtOAc (2 x 200 mL). The filtrate was concentrated and the residue was purified by silica gel column chromatography (5:1 → 2:1, PE:EtOAc) to gain **38** (12.1 g, 47.0 mmol, yield 81%), R_F = 0.2 (19:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.16 (d, *J* = 4.5 Hz, 1H, H-1), 4.41 (d, *J* = 4.6 Hz, 1H, H-2), 4.38 (d, *J* = 0.7 Hz, 1H, H-4), 4.37 (td, *J* = 2.5, 0.6 Hz, 1H, H-5), 4.06 (d, *J* = 0.7 Hz, 1H, H-6a), 4.05 – 4.03 (m, 1H, H-6b), 1.48 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.36 (s, 6H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.9 (C=O), 114.3 (C_q isopropyl), 110.4 (C_q isopropyl), 103.1 (C-1), 78.9 (C-4), 77.2 (C-2), 76.4 (C-5), 64.3 (C-6), 27.6, 27.2, 26.0, 25.3 (4 x CH_3).

1,2:5,6-Di-*O*-isopropylidene-α-D-*allo*-furanoside (39):



38 (12.1 g, 47.0 mmol) was dissolved in a mixture of water and ethanol (72 mL, 4:5). In small portions $NaBH_4$ (8.70 g, 230 mmol) was added. After stirred for 7 hours, the reaction mixture was extracted with DCM (3 x). The combined organic layers were washed with water and brine, dried (Na_2SO_4), filtered, concentrated and the residue was purified by silica gel column chromatography (5:1 → 3:2, PE:EtOAc), to give **39** (11.2 g, 43.1 mmol, yield 92%). R_F = 0.4 (1:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 (d, *J* = 3.8 Hz, 1H, H-1), 4.62 (dd, *J* = 5.2, 3.8 Hz, 1H, H-2), 4.31 (td, *J* = 6.6, 4.7 Hz, 1H, H-5), 4.09 (dd, *J* = 8.5, 6.6 Hz, 1H, H-6a), 4.02 (dd, *J* = 8.5, 6.6 Hz, 1H, H-6b), 3.82 (dd, *J* = 8.5, 4.7 Hz, 1H, H-4), 2.55 (br s, 1H, -OH), 1.58 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 1.38 (d, *J* = 5.2 Hz, 6H, 2 x CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 113.0 (C_q isopropyl), 110.0 (C_q isopropyl), 104.1 (C-1), 79.9 (C-4), 79.1 (C-2), 75.7 (C-5), 72.7 (C-3), 66.0 (C-6), 26.7, 26.7, 26.5, 25.4 (4 x CH_3).

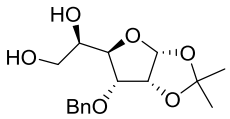
3-*O*-Benzyl-1,2:5,6-di-*O*-isopropylidene-α-D-*allo*-furanoside (40):



NaH (60% on mineral oil, 0.042 g, 1.05 mmol) was added to a solution of **39** (0.14 g, 0.54 mmol) in DMF (2 mL) at 0 °C under argon atmosphere. The mixture was stirred for 1 hour, subsequently, BnBr (0.1 mL, 0.84 mmol) was added. The suspension was stirred overnight at r.t. The

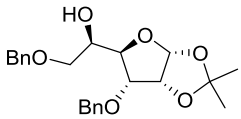
reaction was quenched by the addition of methanol (3 mL), and volatiles were evaporated. The residue was dissolved with EtOAc (10 mL), washed with brine (3 x), dried (Na_2SO_4), filtered, concentrated and purified by silica gel column chromatography to give **40** (0.17 g, 0.48 mmol, yield 90%). R_F = 0.8 (1:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.76 (d, *J* = 3.7 Hz, 1H, H-1), 4.78 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.60 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.59 (t, *J* = 4.2 Hz, 1H, H-2), 4.37 (td, *J* = 7.0, 3.2 Hz, 1H, H-5), 4.15 (dd, *J* = 8.7, 3.2 Hz, 1H, H-4), 4.02 (dd, *J* = 8.3, 6.9 Hz, 1H, H-6a), 3.97 (dd, *J* = 8.3, 7.1 Hz, 1H, H-6b), 3.90 (d, *J* = 4.5 Hz, 1H, H-3), 1.60 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 1.37 (s, 4H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.5 (C_q Bn), 128.4, 128.2, 128.0 (CH_{Ar} Bn), 112.9 (C_q isopropyl), 109.6 (C_q isopropyl), 103.9 (H-1), 78.0 (C-4), 77.8 (C-2), 77.5 (C-3), 74.8 (C-5), 72.2 (CH_2 Bn), 65.0 (C-6), 26.8, 26.6, 26.2, 25.1 (4 x CH_3).

3-*O*-Benzyl-1,2-di-*O*-isopropylidene-α-D-*allo*-furanoside (41):



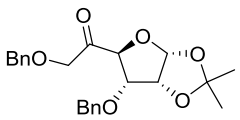
41 was synthesized from **40** (9.0 g, 25.68 mmol) in a yield of 46% (3.67 g, 11.8 mmol), as described for the synthesis of **11**. R_F = 0.15 (1:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.31 (m, 5H, H_{Ar} Bn), 5.79 (d, *J* = 3.7 Hz, 1H, H-1), 4.81 (d, *J* = 11.3 Hz, 1H, CH*H* Bn), 4.63 (t, *J* = 4.1 Hz, 1H, H-2), 4.58 (d, *J* = 11.3 Hz, 1H, CH*H* Bn), 4.13 (dd, *J* = 8.9, 3.4 Hz, 1H, H-4), 4.07 – 4.00 (m, 1H, H-5), 3.96 (dd, *J* = 8.9, 4.4 Hz, 1H, H-3), 3.77 – 3.64 (m, 2H, H-6), 1.62 (s, 3H, CH_3), 1.39 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.7 (C_q Bn), 128.6, 128.4, 128.3 (CH_{Ar} Bn), 113.2 (C_q isopropyl), 104.2 (C-1), 79.1 (C-4), 77.4 (C-2), 76.8 (C-3), 72.2 (CH_2 Bn), 70.1 (C-5), 63.1 (C-6), 26.8, 26.6 (2 x CH_3).

3,6-Di-*O*-Benzyl-1,2-di-*O*-isopropylidene-α-D-*allo*-furanose (42):



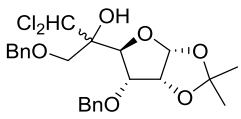
42 was synthesized from **41** (0.45 g, 1.45 mmol) in a yield of 76% (0.44 g, 1.10 mmol), as thick yellow oil, as described for the synthesis of **12**. R_F = 0.27 (10:3, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.30 (m, 10H, H_{Ar} Bn), 5.75 (d, *J* = 3.7 Hz, 1H, H-1), 4.74 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.57 – 4.54 (m, 3H, 2 x CH*H* Bn, H-2), 4.56 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.15 (m, 1H, H-5), 4.14 – 4.09 (m, 1H, H-4), 3.98 (dd, *J* = 8.7, 4.4 Hz, 1H, H-3), 3.60 – 3.55 (m, 2H, H_2-6), 1.61 (s, 3H, CH_3), 1.37 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.0, 137.5 (C_q Bn), 128.5 – 127.6 (CH_{Ar} Bn), 113.0 (C_q isopropyl), 104.2 (C-1), 78.5 (C-4), 77.7 (C-2), 77.1(C-3), 73.4, 72.1 (CH_2 Bn), 70.7 (C-6), 70.1 (C-5), 26.9, 26.7 (2 x CH_3).

1,2-*O*-Isopropyl-3,6-di-*O*-benzyl-α-D-*ribo*-hexofurano-5-ulose (43):



43 was synthesized from **42** (14.0 g, 35.0 mmol) in a yield of 64% (8.91 g, 22.4 mmol), as described for the synthesis of **13**. R_F = 0.4 (10:3, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.21 (m, 10H, H_{Ar} Bn), 5.77 (d, *J* = 3.5 Hz, 1H, H-1), 4.72 (d, *J* = 12.0 Hz, 1H, CH*H* Bn), 4.63 – 4.55 (m, 4H, 2 x CH*H* Bn, H-6, H-4), 4.54 – 4.52 (m, 1H, H-2), 4.31 (d, *J* = 5.0 Hz, 2H, CH_2 Bn), 3.82 (dd, *J* = 9.0, 4.3 Hz, 1H, H-3), 1.58 (s, 3H, CH_3), 1.35 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.8 (C=O), 137.1, 136.9 (C_q Bn), 128.6 – 128.0 (CH_{Ar} Bn), 113.7 (C_q), 104.6 (C-1), 80.4 (C-4), 79.3 (C-3), 77.7 (C-2), 73.3 (CH_2 Bn), 72.8 (C-6), 72.4 (CH_2 Bn), 26.9, 26.6 (2 x CH_3).

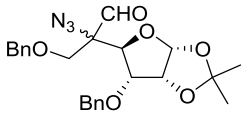
1,2-*O*-Isopropyl-3,6-di-*O*-benzyl-5-*C*-dichloroemethyl-α-D-*allo*/β-L-talo-furanoside (44):



44 was synthesized from **43** (10.0 g, 25.1 mmol) in a yield of 99% (12.0 g, 24.8 mmol) as two inseparable isomers (ratio 1:1) as described for the synthesis of **14**. R_F = 0.63 (5:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.31 (m, 10H, H_{Ar} Bn), 6.12 (s, 1H, C*H*Cl_2), 5.78 (d, *J* = 3.6 Hz, 1H, H-1), 4.70 (d, *J* = 11.5 Hz, 1H, CH*H* Bn), 4.58 – 4.52 (m, 3H, H_2-6, H-2), 4.49 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.41 (d, *J* = 8.3 Hz, 1H, H-4), 4.12 (dd, *J* = 8.3, 4.4 Hz, 1H, H-3), 3.90 (d, *J* = 10.2 Hz, 1H, CH*H* Bn), 3.74 (d, *J* = 10.2 Hz, 1H, CH*H* Bn), 1.60 (s, 3H, CH_3), 1.38 (s, 3H,

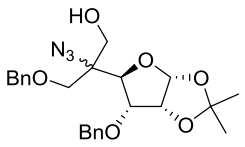
CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.3, 137.3 (C_q Bn), 128.5, 128.4, 128.4, 128.2, 128.1, 128.1, 128.0, 127.9, 127.8, 127.8 (CH_{Ar} Bn), 113.5 (C_q isopropyl), 104.1 (C-1), 78.9 (C-4), 77.9 (C-2), 77.8 (C-3), 76.1 (C-5), 75.8 ($CHCl_2$), 73.8 (C-6), 72.1 (CH_2 Bn), 67.1 (CH_2 Bn), 27.1, 26.9 (2 x CH_3).

5-Deoxy-5-azido-5-*C*-benzyloxymethyl-3-*O*-benzyl-1,2-*O*-isopropyl-α-D-*allo*/β-L-*talo*-furano-1,6-dialdose (45):



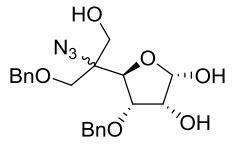
45 was synthesized from **44** (12.0 g, 24.8 mmol) in a yield of 71% (7.99 g, 17.6 mmol), as described for the synthesis of **15**. R_F = 0.25 (10:1, PE:EtOAc). **45** is an inseparable mixture of diastereomers (ratio = 5:3). NMR data of the major diastereomer: ^1H NMR (400 MHz, $CDCl_3$) δ 9.52 (s, 1H, CHO), 7.50 – 7.20 (m, 10H, H_{Ar} Bn), 5.73 (d, *J* = 3.5 Hz, 1H, H-1), 4.64 – 4.42 (m, 5H, 2 x CH*H* Bn, H_2-6, H-2), 4.35 (d, *J* = 8.7 Hz, 1H, H-4), 4.12 (d, *J* = 10.0 Hz, 1H, CH*H* Bn), 3.99 (d, *J* = 10.0 Hz, 1H, CH*H* Bn), 3.97 (dd, *J* = 8.7, 4.3 Hz, 1H, H-3), 1.59 (s, 3H, CH_3), 1.35 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.7 (CHO), 137.0, 136.7 (C_q Bn), 128.6 – 127.7 (CH_{Ar} Bn), 113.6 (C_q isopropyl), 104.6 (C-1), 77.8 C-4), 77.2 (C-3), 76.9 (C-2), 73.8 (C-6), 72.4, 71.0 (2 x CH_2 Bn), 69.5 (C-5), 26.9, 26.4 (2 x CH_3).

5-Deoxy-5-azido-5-*C*-benzyloxymethyl-3-*O*-benzyl-1,2-*O*-isopropyl-α-D-*allo*/β-L-*talo*-furanoside (46):



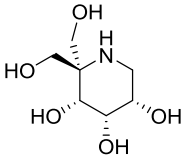
46 was synthesized from **45** (7.46 g, 16.5 mmol) in a yield of 81% (6.06 g, 13.3 mmol) as two inseparable diastereomers as described for the synthesis of **16**. R_F = 0.23 (9:1, PE:EtOAc). NMR-data of the major diastereomer: ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.30 (m, 10H, H_{Ar} Bn), 5.82 (d, *J* = 3.7 Hz, 1H, H-1), 4.81 (d, *J* = 11.0 Hz, 1H, CH*H* Bn), 4.67 – 4.60 (m, 3H, H_2-6, H-2), 4.58 (d, *J* = 11.0 Hz, 1H, CH*H* Bn), 4.22 (d, *J* = 8.6 Hz, 1H, H-4), 4.11 – 4.08 (m, 1H, H-3), 3.93 (d, *J* = 9.9 Hz, 1H, CH*H* Bn), 3.86 (d, *J* = 9.9 Hz, 1H, CH*H* Bn), 3.86 (d, *J* = 9.9 Hz, 1H, CH*H*OH), 3.67 (dd, *J* = 9.9, 3.7 Hz, 1H, CH*H*OH), 1.60 (s, 3H, CH_3), 1.41 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.7, 136.4 (C_q Bn), 128.7 – 127.7 (CH_{Ar} Bn), 113.4 (C_q isopropyl), 104.3 (C-1), 79.5 (C-4), 77.8 (C-3), 77.2 (C-2), 73.7 (C-6), 72.3, 69.9 (CH_2 Bn), 66.6 (C-5), 62.3 (CH_2OH), 26.9, 26.7 (2 x CH_3).

5-Deoxy-5-azido-5-*C*-benzyloxymethyl-3-*O*-benzyl-α-D-*allo*/β-L-*talo*-furanoside (47):



47 was synthesized from **46** (1.40 g, 3.07 mmol) in a yield of 70% (0.89 g, 2.15 mmol), as two inseparable diastereoisomer (ratio = 5:3) as described for the synthesis of **17**. R_F = 0.15 (5:3, PE:EtOAc). NMR data of the major diastereomer: ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.31 (m, 10H, H_{Ar} Bn), 5.29 (s, 1H, H-1), 4.71 – 4.38 (m, 5H, CH_2 Bn, H_2-6, H-2), 4.30 – 4.23 (m, 1H, H-4), 4.08 – 4.03 (m, 1H, H-3), 3.81 – 3.73 (m, 2H, CH_2 Bn), 3.69 – 3.51 (m, 2H, C*H*$_2$OH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.6 – 127.7 (CH_{Ar} Bn), 96.9 (C-1), 81.5 (C-4), 77.9 (C-2), 77.0 (C-3), 73.8 (C-6), 72.9 (CH_2 Bn), 69.5 (CH_2 Bn), 66.6 (C-5), 62.9 (CH_2OH).

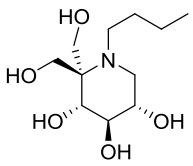
5-*C*-Hydroxymethyl-1-deoxy-D-allonojirimycin (9):



9 was synthesized from **47** (0.79 g, 1.90 mmol) in a yield of 81% (0.30 g, 1.54 mmol) as described for the synthesis of **6**. ^1H NMR (400 MHz, MeOD) δ 4.02 (d, *J* = 11.5 Hz, 1H, H-6a), 3.98 (t, *J* = 3.2 Hz, 1H, H-3), 3.81 (d, *J* = 3.2 Hz, 1H, H-4), 3.75 – 3.71 (m, 1H, H-2), 3.73 (d, *J* = 10.8Hz, 1H, H-6*a), 3.67 (d, *J* = 11.6 Hz, 1H, H-6b), 3.59 (d, *J* = 11.1 Hz, 1H, H-6*b), 3.03 (dd, *J* = 13.1, 8.2 Hz, 1H, H-1a), 2.87 (dd, *J* = 13.1, 4.0 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, MeOD) δ 70.0 (C-3), 69.5 (C-4), 68.3 (C-2), 61.3 (C-6), 60.8 (C-6*), 60.3 (C-5), 42.3 (C-1). $[\alpha]^{20}_D$ = +0.23 (c =1.31, MeOH). IR/cm^{-1}: 3263, 2900, 1607, 1450, 1413, 1257, 1033. HRMS: found 194.10218 $[M+H]^+$, calculated for $[C_7H_{15}NO_5+H]^+$ 194.10230.

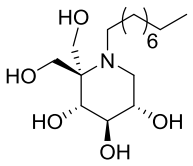
N-Alkylated final compounds:

5-*C*-Hydroxymethyl-*N*-butyl-1-deoxynojirimycin (56):



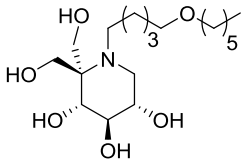
6 (0.10 mmol) and butyl bromide (0.16 mmol) was subjected to general alkylation procedure to provide **56** (0.5 mg, 0.002 mmol, yield 2%). ^{1}H NMR (600 MHz, MeOD) δ 4.04 (d, *J* = 13.3 Hz, 1H, H-6a), 3.90 (d, *J* = 12.0 Hz, 1H, H-6*a), 3.87 (d, *J* = 12.9 Hz, 1H, H-6b), 3.86 (t, *J* = 9.6 Hz, 1H, H-3), 3.78 (d, *J* = 12.0 Hz, 1H, H-6*b), 3.76 – 3.72 (m, 1H, H-2), 3.68 (d, *J* = 10.0 Hz, 1H, H-4), 3.59 – 3.51 (m, 2H, H-1a, H-1'a), 3.47 – 3.43 (m, 1H, H-1b), 3.14 (td, *J* = 12.3, 5.0 Hz, 1H, H-1'b), 1.93 – 1.83 (m, 1H, H-2'a), 1.78 – 1.68 (m, 1H, H-2'b), 1.53 – 1.41 (m, 2H, H_2-3'), 1.04 (t, *J* = 7.4 Hz, 3H, H_3-4'). ^{13}C NMR (150 MHz, MeOD) δ 74.1 (C-3), 72.9 (C-5), 70.0 (C-4), 67.9 (C-2), 56.8 (C-6*), 56.5 (C-6), 52.6 (C-1), 52.5 (C-1'), 27.9 (C-2'), 20.7 (C-3'), 13.5 (C-4'). IR/cm^{-1}: 3471, 2970, 1738, 1442, 1365, 1216, 1139. $[\alpha]^{20}_D$ = -2.00 (c = 0.01, MeOH). HRMS: found 250.16502 $[C_{11}H_{23}NO_5+H]^+$, calculated for $[C_{11}H_{23}NO_5+H]^+$ 250.16490.

5-*C*-Hydroxymethyl-*N*-nonyl-1-deoxynojirimycin (57):



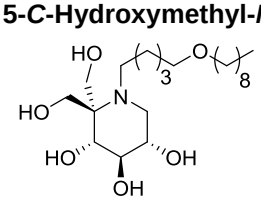
6 (0.20 mmol) and nonyl bromide (0.31 mmol) was subjected to general alkylation procedure to provide **57** (5.0 mg, 0.016 mmol, yield 8%). ^{1}H NMR (600 MHz, MeOD) δ 4.04 (d, *J* = 13.3 Hz, 1H, H-6a), 3.90 (d, *J* = 12.0 Hz, 1H, H-6*a), 3.86 (d, *J* = 13.6 Hz, 1H, H-6b), 3.86 (t, *J* = 10.0 Hz, 1H, H-3), 3.77 (d, *J* = 11.9 Hz, 1H, H-6*b), 3.78 – 3.71 (m, 1H, H-2), 3.68 (d, *J* = 10.0 Hz, 1H, H-4), 3.58 – 3.50 (m, 2H, H-1a, H-1'a), 3.44 (t, *J* = 11.7 Hz, 1H, H-1b), 3.12 (td, *J* = 12.3, 5.0 Hz, 1H, H-1'b), 1.96 – 1.83 (m, 1H, H-2'a), 1.80 – 1.70 (m, 1H, H-2'b), 1.47 – 1.25 (m, 12H, H_2-3', H_2-4', H_2-5', H_2-6', H_2-7', H_2-8'), 0.93 (t, *J* = 7.1 Hz, 3H, H_3-9'). ^{13}C NMR (150 MHz, MeOD) δ 74.0 (C-3), 72.9 (C-5), 70.0 (C-4), 67.9 (C-2), 56.8 (C-6*), 56.5 (C-6), 52.6 (C-1'), 52.6 (C-1), 32.6 , 30.1, 29.9, 29.9, 27.4, 25.9, 23.3, 14.0 (C-2' – C-9'). IR/cm^{-1}: 3675, 2988, 2901, 1677, 1394, 1226, 1056. $[\alpha]^{20}_D$ = -0.1 (c = 0.10, MeOH). HRMS: found 320.24321 $[C_{16}H_{33}NO_5+H]^+$, calculated for $[C_{16}H_{33}NO_5+H]^+$ 320.24315.

5-*C*-Hydroxymethyl-*N*-[5-(hexyloxy)pentyl]-1-deoxynojirimycin (58):



6 (0.20 mmol) and pentyloxyhexyl bromide (0.30 mmol) was subjected to general alkylation procedure to provide **58** (3.0 mg, 0.008 mmol, yield 4%). ^{1}H NMR (600 MHz, MeOD) δ 4.02 (d, *J* = 13.3 Hz, 1H, H-6a), 3.88 (d, *J* = 12.0 Hz, 1H, H-6*a), 3.84 (t, *J* = 9.6 Hz, 1H, H-3), 3.84 (d, *J* = 13.2 Hz, 1H, H-6b), 3.75 (d, *J* = 11.9 Hz, 1H, H-6*b), 3.75 – 3.69 (m, 1H, H-2), 3.66 (d, *J* = 10.0 Hz, 1H, H-4), 3.56 – 3.50 (m, 2H, H-1a, H-1'a), 3.44 – 3.40 (m, 1H, H-1b), 3.46 (t, *J* = 6.3 Hz, 2H, H_2-5'), 3.43 (t, *J* = 6.7 Hz, 2H, H_2-6'), 3.12 (td, *J* = 12.2, 5.0 Hz, 1H, H-1'b), 1.94 – 1.86 (m, 1H, H-2'a), 1.81 – 1.69 (m, 1H, H-2'b), 1.68 – 1.60 (m, 2H, H_2-4'), 1.60 – 1.53 (m, 2H, H_2-7'), 1.52 – 1.43 (m, 2H, H_2-3'), 1.40 – 1.26 (m, 6H, H_2-8', H_2-9', H_2-10'), 0.91 (t, *J* = 6.9 Hz, 3H, H_3-11'). ^{13}C NMR (150 MHz, MeOD) δ 74.4 (C-3), 73.3 (C-5), 72.1 (C-6'), 71.4 (C-5'), 70.4 (C-4), 68.2 (C-2), 57.2 (C-6), 56.9 (C-6*), 53.0 (C-1), 52.9 (C-1'), 32.9 (C-9'), 30.7 (C-7'), 30.2 (C-4'), 27.0 (C-8'), 26.1 (C-2'), 24.6 (C-3'), 23.7 (C-10'), 14.4 (C-11'). IR/cm^{-1}: 3316, 2933, 1673, 1439, 1366, 1205, 1135. $[\alpha]^{20}_D$ = -1.00 (c = 0.06, MeOH). HRMS: found 364.26940 $[C_{18}H_{37}NO_6+H]^+$, calculated for $[C_{18}H_{37}NO_6+H]^+$ 364.26936.

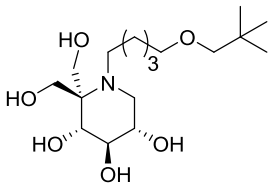
5-*C*-Hydroxymethyl-*N*-[5-(nonyloxy)pentyl]-1-deoxynojirimycin (59):



6 (0.20 mmol) and pentyloxynonyl bromide (0.30 mmol) was subjected to general alkylation procedure to provide **59** (2.4 mg, 0.006 mmol, yield 3%). ^{1}H NMR (600 MHz, MeOD) δ 4.02 (d, *J* = 13.3 Hz, 1H, H-6a), 3.88 (d, *J* = 12.0 Hz, 1H, H-6*a), 3.84 (t, *J* = 9.6 Hz, 1H, H-3), 3.84 (d, *J* = 13.8 Hz, 1H, H-6b), 3.74 (d, *J* = 12.0 Hz, 1H, H-6*b), 3.73 – 3.69

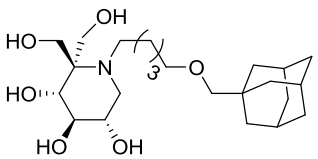
(m, 1H, H-2), 3.66 (d, *J* = 10.0 Hz, 1H, H-4), 3.57 – 3.49 (m, 2H, H-1a, H-1'a), 3.46 (t, *J* = 6.3 Hz, 2H, H_2-5'), 3.43 (t, *J* = 6.6 Hz, 2H, H_2-6'), 3.44 – 3.40 (m, 1H, H-1b), 3.12 (td, *J* = 12.2, 5.0 Hz, 1H, H-1'b), 1.90 (ddt, *J* = 20.9, 12.1, 5.8 Hz, 1H, H-2'a), 1.75 (dtt, *J* = 22.4, 12.0, 5.1 Hz, 1H, H-2'b), 1.68 – 1.61 (m, 2H, H_2-4'), 1.59 – 1.53 (m, 2H, H_2-7'), 1.53 – 1.42 (m, 2H, H_2-3'), 1.40 – 1.23 (m, 12H, H_2-8', H_2-9', H_2-10', H_2-11', H_2-12', H_2-13'), 0.90 (t, *J* = 7.0 Hz, 3H, H_3-14'). ^{13}C NMR (150 MHz, MeOD) δ 74.4 (C-3), 73.3 (C-5), 72.1 (C-6'), 71.4(C-5'), 70.4 (C-4), 68.2 (C-2), 57.2 (C-6), 56.9 (C-6*), 53.0 (C-1), 52.9 (C-1'), 33.1 (C-9'), 30.8 (C-7'), 30.7, 30.6 30.4 (C-10', C-11', C-12'), 30.2 (C-4'), 27.3 (C-8'), 26.1 (C-2'), 24.6 (C-3'), 23.7 (C-13'), 14.4 (C-14'). $[\alpha]^{20}_D$ = -0.63 (c = 0.05, MeOH). IR/cm^{-1}: 3357, 2928, 1738, 1676, 1438, 1365, 1216, 1137, 801, 724, 527. HRMS: found 406.31624 $[C_{21}H_{43}NO_6+H]^+$, calculated for $[C_{21}H_{43}NO_6+H]^+$ 406.31631.

5-*C*-Hydroxymethyl-*N*-[5-(3,3-dimethyl-1-propyloxy)pentyl]-1-deoxynojirimycin (60):



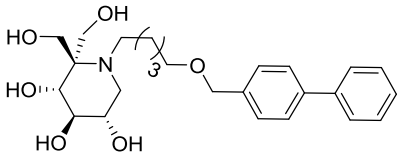
6 (0.10 mmol) and 1-bromo-5-(2,2-dimethyl-1-propoxy) pentane (0.15 mmol) was subjected to general alkylation procedure to provide **60** (1.1 mg, 0.0032 mmol, yield 3%). ^{1}H NMR (600 MHz, MeOD) δ 4.02 (d, *J* = 13.3 Hz, 1H, H-6a), 3.88 (d, *J* = 12.0 Hz, 1H, H-6*a), 3.84 (d, *J* = 13.3 Hz, 1H, H-6b), 3.75 (d, *J* = 12.0 Hz, 1H, H-6*b), 3.86 – 3.81 (m, 1H, H-3), 3.75 – 3.69 (m, 1H, H-2), 3.65 (d, *J* = 10.0 Hz, 1H, H-4), 3.56 – 3.50 (m, 2H, H-1a, H-1'a), 3.45 (t, *J* = 6.3 Hz, 2H, H_2-5'), 3.44 – 3.38 (m, 1H, H-1b), 3.12 (td, *J* = 12.2, 5.0 Hz, 1H, H-1'b), 3.08 (s, 2H, H_2-6'),1.94 – 1.89 (m, 1H, H-2'a), 1.77 – 1.73 (m, 1H, H-2'b), 1.69 – 1.65 (m, 2H, H_2-3'), 1.61 – 1.42 (m, 2H, H_2-4'), 0.91 (s, 9H, 3 x CH_3). ^{13}C NMR (150 MHz, MeOD) δ 82.6 (C-6'), 74.4 (C-3), 73.3 (C-5), 72.0 (C-5'), 70.4 (C-4), 68.2 (C-2), 57.2 (C-6), 56.9 (C-6*), 53.0 (C-1), 53.0 (C-1'), 32.9 (C_q), 30.3 (C-4'), 27.1 (C-2'), 26.2 (C-3'), 24.6 (3 x CH_3). $[\alpha]^{20}_D$ = -1.36 (c = 0.02, MeOH). IR/cm^{-1}: 3460, 3016, 2970, 1738, 1442, 1365, 1216, 1132. HRMS: found 350.25376 $[C_{17}H_{35}NO_6+H]^+$, calculated for $[C_{17}H_{35}NO_6+H]^+$ 350.25371.

5-*C*-Hydroxymethyl-*N*-[5-(adamantan-1-yl-methoxy)-pentyl]-1-deoxynojirimycin (61):



6 (0.20 mmol) and 5-(adamantan-1-yl-methoxy)pentyl bromide (0.29 mmol) was subjected to general alkylation procedure to provide **61** (9.1 mg, 0.022 mmol, yield 11%). ^{1}H NMR (600 MHz, MeOD) δ 4.02 (d, *J* = 13.4 Hz, 1H, H-6a), 3.88 (d, *J* = 12.2 Hz, 1H, H-6b), 3.85 (d, *J* = 13.8 Hz, H-6*a), 3.86 – 3.82 (m, 1H, H-3), 3.76 (d, *J* = 12.2 Hz, 1H, H-6*b), 3.76 – 3.72 (m, 1H, H-2), 3.66 (d, *J* = 10.0 Hz, 1H, H-4), 3.55 – 3.50 (m, 2H, H-1a, H-1'a), 3.42 (t, *J* = 6.3 Hz, 2H, H_2-5'), 3.43 – 3.39 (m, 1H, H- 1b) 3.16 – 3.08 (m, 1H, H-1'b), 2.99 (s, 2H, H_2-6'), 1.94 (p, *J* = 3.0 Hz, 3H, 3 x CH ada), 1.94 – 1.90 (m, 1H, H-2'a), 1.77 – 1.66 (m, 7H, 3 x CH_2 ada, H-2'b), 1.63 (m, 2H, H_2-4'), 1.56 (d, *J* = 2.9 Hz, 6H, 3 x CH_2 ada), 1.53 – 1.41 (m, 2H, H_2-3'). ^{13}C NMR (150 MHz, MeOD) δ 83.1 (C-6'), 74.4 (C-3), 73.2 (C-5), 72.1 (C-5'), 70.4 (C-4), 68.2 (C-2), 57.2 (C-6), 56.9 (C-6*), 53.0 (C-1'), 52.9 (C-1), 40.8 (CH_2 ada), 38.3 (CH_2 ada), 35.1 (C_q ada), 30.1 (C-4'), 29.7 (CH ada), 26.1 (C-2'), 24.6 (C-3'). $[\alpha]^{20}_D$ = -0.77 (c = 0.18, MeOH). IR/cm^{-1}: 3346, 2902, 2848, 1738, 1673, 1448, 1365, 1205, 1136. HRMS: found 428.30048 $[C_{23}H_{41}NO_6+H]^+$, calculated for $[C_{23}H_{41}NO_6+H]^+$ 428.30066.

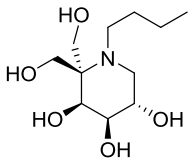
5-*C*-Hydroxymethyl-*N*-[(biphenyl-4-yl-methoxy)-pentyl]-1-deoxynojirimycin (62):



6 (0.20 mmol) and (biphenyl-4-yl-methoxy)pentyl bromide (0.30 mmol) was subjected to general alkylation procedure to provide **62** (40.8 mg, 0.092 mmol, yield 46%). ^{1}H NMR (600 MHz, MeOD) δ 7.63 (dd, *J* = 8.3, 1.7 Hz, 4H, H_{Ar} BiPh), 7.48 – 7.41 (m, 4H, H_{Ar} BiPh), 7.39 – 7.32 (m, 1H, H_{Ar} BiPh), 4.58 (s, 2H, H_2-6'), 4.03 (d, *J* = 13.3 Hz, 1H, H-6a), 3.90 (d, *J* = 12.1 Hz, 1H, H-6*a), 3.86 (d, *J* = 10.1 Hz, 1H, H-3), 3.86 (d, *J* = 13.2 Hz, 1H, H-6b), 3.77 (d, *J* = 12 Hz, 1H, H-6*b), 3.77 – 3.63 (m, 1H, H-2), 3.68 (d, *J* = 10.0 Hz, 1H, H-4), 3.59

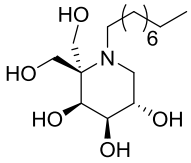
(t, *J* = 6.2 Hz, 2H, H_2-5'), 3.57 – 3.51 (m, 2H, H-1a, H-1'a), 3.44 (t, *J* = 11.8 Hz, 1H, H-1b), 3.15 (td, *J* = 12.2, 5.0 Hz, 1H, H-1'b), 2.01 – 1.86 (m, 1H, H-2'a), 1.84 – 1.76 (m, 1H, H-2'b), 1.76 – 1.69 (m, 2H, H_2-4'), 1.64 – 1.45 (m, 2H, H_2-3'a). ^{13}C NMR (150 MHz, MeOD) δ 141.7, 141.5 (C_q BiPh), 138.5 – 127.5 (C_{Ar} BiPh), 74.1 (C-3), 73.3 (C-6'), 72.9 (C-5), 70.6 (C-5'), 70.1 (C-4), 67.9 (C-2), 56.8 (C-6), 56.5 (C-6*), 52.6 (C-1), 52.6 (C-2), 29.8 (C-4'), 25.7 (C-2'), 24.3 (C-3'). $[\alpha]^{20}_D$ = -0.1 (c = 0.82, MeOH). IR/cm^{-1}: 3361, 3016, 2970, 1738, 1675, 1440, 1365, 1205, 1134. HRMS: found 446.25357 $[C_{25}H_{35}NO_6+H]^+$, calculated for $[C_{25}H_{35}NO_6+H]^+$ 446.25371.

5-*C*-Hydroxymethyl-*N*-butyl-1-deoxy-D-galactonojirimycin (77):



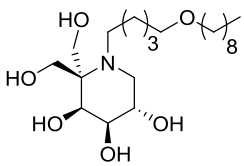
7 (0.20 mmol) and butyl bromide (0.30 mmol) was subjected to general alkylation procedure to provide **77** (11.2 mg, 0.044 mmol, yield 22%). ^{1}H NMR (600 MHz, MeOD) δ 4.27 (d, *J* = 3.4 Hz, 1H, H-4), 4.24 (d, *J* = 14.0 Hz, 1H, H-6a), 4.00 (td, *J* = 4.8, 1.8 Hz, 1H, H-2), 3.98 (d, *J* = 11.4 Hz, 1H, H-6*a), 3.94 (t, *J* = 4.1 Hz, 1H, H-3), 3.89 (d, *J* = 12 Hz, 1H, H-6*b), 3.89 (d, *J* = 14.4 Hz, 1H, H-6b), 3.76 (dd, *J* = 13.1, 1.6 Hz, 1H, H-1a), 3.62 (ddd, *J* = 13.1, 10.1, 6.6 Hz, 1H, 1'a), 3.42 (dd, *J* = 13.8, 3.6 Hz, 1H, H-1b), 3.24 – 3.17 (m, 1H, H-1'b), 1.89 – 1.79 (m, 1H, H-2'a), 1.74 – 1.64 (m, 1H, H-2'b), 1.52 – 1.36 (m, 2H, H_2-3'), 1.01 (t, *J* = 7.4 Hz, 3H, H_3-4'). ^{13}C NMR (150 MHz, MeOD) δ 73.6 (C-5), 70.2 (C-3), 66.8 (C-2), 65.1 (C-4), 56.9 (C-6*), 56.5 (C-6), 51.8 (C-1'), 49.5 (C-1), 28.5 (C-2'), 20.0 (C-3'), 13.5 (C-4'). $[\alpha]^{20}_D$ = +0.04 (c = 0.22, MeOH). IR/cm^{-1}: 3271, 2968, 2879, 1674, 1435, 1201, 1134, 1082. HRMS: found 250.16488 $[C_{11}H_{23}NO_5+H]^+$, calculated for $[C_{11}H_{23}NO_5+H]^+$ 250.16490.

5-*C*-Hydroxymethyl-*N*-nonyl-1-deoxy-D-galactonojirimycin (78):



7 (0.20 mmol) and nonyl bromide (0.30 mmol) was subjected to general alkylation procedure to provide **78** (11.8 mg, 0.036 mmol, yield 18%). ^{1}H NMR (400 MHz, MeOD) δ 4.30 (d, *J* = 3.3 Hz, 1H, H-4), 4.27 (d, *J* = 14.0 Hz, 1H, H-6a), 4.04 – 4.00 (m, 1H, H-2), 4.00 (d, *J* = 11.9 Hz, 1H, H-6*a), 3.98 – 3.95 (m, 1H, H-3), 3.91 (d, *J* = 11.5 Hz, 1H, H-6*b), 3.91 (d, *J* = 14.2 Hz, 1H, H-6b), 3.78 (dd, *J* = 13.0, 1.6 Hz, 1H, H-1a), 3.63 (ddd, *J* = 13.0, 10.0, 6.7 Hz, 1H, H-1'a), 3.43 (dd, *J* = 13.1, 3.4 Hz, 1H, H-1b), 3.23 (ddd, *J* = 13.6, 9.6, 4.9 Hz, 1H, H-1'b), 1.96 – 1.82 (m, 1H, H-2'a), 1.80 – 1.66 (m, 1H, H-2'b), 1.51 – 1.28 (m, 12H, H_2-3', H_2-4', H_2-5', H_2-6', H_2-7', H_2-8'), 0.93 (t, *J* = 7.1 Hz, 3H, H_3-9'). ^{13}C NMR (100 MHz, MeOD) δ 72.6 (C-5), 69.2 (C-3), 65.8 (C-2), 64.1 (C-4), 55.8 (C-6*), 55.4 (C-6), 51.0 (C-1'), 48.4 (C-1), 31.6, 29.1, 28.9, 28.8, 25.7, 25.4, 22.3 (C-2' – C-8'), 13.0 (C-9'). $[\alpha]^{20}_D$ = +0.0 (c = 0.24, MeOH). IR/cm^{-1}: 3336, 2928, 1738, 1673, 1438, 1365, 1204, 1136, 1080. HRMS: found 320.24316 $[C_{16}H_{33}NO_5+H]^+$, calculated for $[C_{16}H_{33}NO_5+H]^+$ 320.24315.

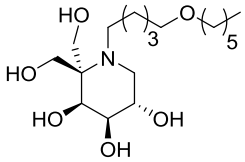
5-*C*-Hydroxymethyl-*N*-[5-(hexyloxy)pentyl]-1-deoxy-D-galactonojirimycin (79):



7 (0.20 mmol) and pentyloxyhexyl bromide (0.30 mmol) was subjected to general alkylation procedure to provide **79** (15.3 mg, 0.042 mmol, yield 21%). ^{1}H NMR (400 MHz, MeOD) δ 4.30 (d, *J* = 3.3 Hz, 1H, H-4), 4.26 (d, *J* = 14.0 Hz, 1H, H-6a), 4.05 – 4.02 (m, 1H, H-2), 4.00 (d, *J* = 12.0 Hz, 1H, H-6*a), 3.98 – 3.95 (m, 1H, H-3), 3.92 (d, *J* = 11.7 Hz, 1H, H-6*b), 3.91 (d, *J* = 14.1 Hz, 1H, H-6b), 3.79 (dd, *J* = 13.1, 1.3 Hz, 1H, H-1a), 3.64 (ddd, *J* = 13.2, 10.1, 6.6 Hz, 1H, H-1'a), 3.48 (t, *J* = 6.3 Hz, 2H, H_2-5'), 3.45 (t, *J* = 6.6 Hz, 2H, H_2-6'), 3.43 (dd, *J* = 13.2, 3.5 Hz, 1H, H-1b), 3.24 (ddd, *J* = 13.0, 9.7, 4.4 Hz, 1H, H-1'b), 1.99 – 1.85 (m, 1H, H-2'a), 1.85 – 1.71 (m, 1H, H-2'b), 1.71 – 1.62 (m, 2H, H_2-4'), 1.57 (dt, *J* = 7.9, 6.6 Hz, 2H, H_2-7'), 1.54 – 1.43 (m, 2H, H_2-3'), 1.42 – 1.28 (m, 6H, H_2-8', H_2-9', H_2-10'), 0.93 (t, *J* = 7.1 Hz, 3H, H_3-11'). ^{13}C NMR (150 MHz, MeOD) δ 71.8 (C-6'), 71.1 (C-5'), 70.5 (C-3), 66.8 (C-2), 65.3 (C-4), 58.4 (C-6*), 57.1(C-6), 52.2 (C-1'), 49.8 (C-1), 32.6 (C-10'), 30.5 (C-7'), 29.9 (C-4'), 26.7 (C-8'), 26.3 (C-2'), 23.9 (C-3'), 23.5 (C-9'), 14.2 (C-10'). $[\alpha]^{20}_D$ = +0.1 (c = 0.31, MeOH). IR/cm^{-1}: 3346, 2931,

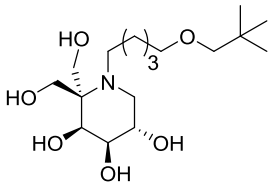
2860, 1670, 1458, 1431, 1201, 1132, 1082. HRMS: found 364.26934 $[C_{18}H_{37}NO_6+H]^+$, calculated for $[C_{18}H_{37}NO_6+H]^+$ 364.26936.

5-*C*-Hydroxymethyl-*N*-[5-(nonyloxy)pentyl]-1-deoxy-D-galactonojirimycin (80):



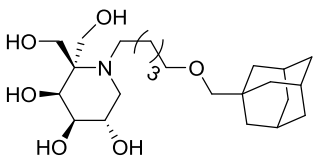
7 (0.20 mmol) and pentyloxynonyl bromide (0.30 mmol) was subjected to general alkylation procedure to provide **80** (11.5 mg, 0.028 mmol, yield 14%). ^{1}H NMR (400 MHz, MeOD) δ 4.29 (d, *J* = 3.3 Hz, 1H, H-4), 4.26 (d, *J* = 14.0 Hz, 1H, H-6a), 4.03 – 4.01 (m, 1H, H-2), 4.00 (d, *J* = 11.8 Hz, 1H, H-6*a), 3.97 – 3.94 (m, 1H, H-3), 3.91 (d, *J* = 11.2 Hz, 1H, H-6*b), 3.91 (d, *J* = 14.2 Hz, 1H, H-6b), 3.79 (dd, *J* = 13.1, 1.6 Hz, 1H, H-1a), 3.69 – 3.56 (m, 1H, H-1'a), 3.47 (t, *J* = 6.2 Hz, 2H, H_2-5'), 3.44 (t, *J* = 6.6 Hz, 2H, H_2-6'), 3.45 – 3.42 (m, 1H, H-1b), 3.23 (ddd, *J* = 14.1, 9.8, 4.4 Hz, 1H, H-1'b), 1.99 – 1.85 (m, 1H, H-2'a), 1.80 – 1.72 (m, 1H, H-2'b), 1.65 (dt, *J* = 8.1, 6.1 Hz, 2H, H_2-4'), 1.60 – 1.53 (m, 2H, H_2-7'), 1.53 – 1.41 (m, 2H, H_2-3'), 1.39 – 1.26 (m, 12H, H_2-8', H_2-9', H_2-10', H_2-11', H_2-12', H_2-13'), 0.93 (t, *J* = 6.8 Hz, 3H, H_3-14'). ^{13}C NMR (100 MHz, MeOD) δ 72.6 (C-5), 70.7 (C-6'), 69.9 (C-5'), 69.2 (C-3), 65.8 (C-2), 64.2 (C-4), 55.9 (C-6*), 55.5 (C-6), 50.9 (C-1'), 48.6 (C-1), 31.6 (C-9'), 29.4 (C-7'), 29.3, 29.2, 29.0 (C-10', C-11', C-12'), 28.7 (C-4'), 25.9 (C-8'), 25.2 (C-2'), 22.6 (C-3'), 22.3 (C-13'), 13.0 (C-14'). IR/cm^{-1}: 3675, 3353, 2971, 2924, 1674, 1394, 1203, 1067. $[\alpha]^{20}_D$ = +0.1 (c = 0.23, MeOH). HRMS: found 406.31615 $[C_{21}H_{43}NO_6+H]^+$, calculated for $[C_{21}H_{43}NO_6+H]^+$ 406.31631.

5-*C*-Hydroxymethyl-*N*-[5-(3,3-dimethyl-1-propyloxy)pentyl]-1-deoxy-D-galactonojirimycin (81):



7 (0.20 mmol) and 1-bromo-5-(2,2-dimethyl-1-propoxy) pentane (0.30 mmol) was subjected to general alkylation procedure to provide **81** (14.3 mg, 0.04 mmol, yield 20%). ^{1}H NMR (400 MHz, MeOD) δ 4.30 (d, *J* = 3.3 Hz, 1H, H-4), 4.27 (d, *J* = 14.1 Hz, 1H, H-6a), 4.02 (td, *J* = 3.6, 1.6 Hz, 1H, H-2), 4.00 (d, *J* = 11.6 Hz, 1H, H-6*a), 3.97 (t, *J* = 3.6 Hz, 1H, H-3), 3.92 (d, *J* = 11.2 Hz, 1H, H-6*b), 3.91 (d, *J* = 14.0 Hz, 1H, H-6b), 3.79 (dd, *J* = 13.1, 1.7 Hz, 1H, H-1a), 3.64 (ddd, *J* = 13.1, 10.1, 6.7 Hz, 1H, H-1'a), 3.47 (t, *J* = 6.1 Hz, 2H, H_2-5'), 3.44 (dd, *J* = 13.2, 3.2 Hz, 1H, H-1b), 3.28 – 3.20 (m, 1H, H-1'b), 3.10 (s, 2H, H_2-6'), 2.03 – 1.88 (m, 1H, H-2'a), 1.85 – 1.74 (m, 1H, H-2'b), 1.71 – 1.63 (m, 2H, H_2-4'), 1.61 – 1.42 (m, 2H, H_2-3'), 0.93 (s, 9H, 3 x CH_3). ^{13}C NMR (100 MHz, MeOD) δ 81.1 (C-6'), 72.6 (C-5), 70.6 (C-5'), 69.2 (C-3), 65.8 (C-2), 64.1 (C-4), 55.9 (C-6*), 55.5 (C-6), 50.9 (C-1'), 48.5 (C-1), 31.5 (C-7'), 28.8 (C-4'), 25.7 (CH_3), 25.3 (C-2'), 22.7 (C-3'). $[\alpha]^{20}_D$ = -0.1, (c = 0.29, MeOH). IR/cm^{-1}: 3675, 3327, 2971, 1673, 1393, 1202, 1066. HRMS: found 350.25364 $[C_{17}H_{35}NO_6+H]^+$, calculated for $[C_{17}H_{35}NO_6+H]^+$ 350.25371.

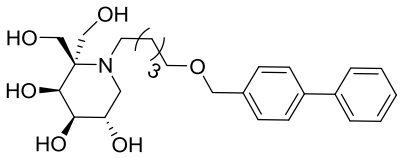
5-*C*-Hydroxymethyl-*N*-[5-(adamantan-1-yl-methoxy)-pentyl]-1-deoxy-D-galactonojirimycin (82):



7 (0.20 mmol) and 5-(adamantan-1-yl-methoxy)pentyl bromide (0.30 mmol) was subjected to general alkylation procedure to provide **82** (36.5 mg, 0.09 mmol, yield 43%). ^{1}H NMR (400 MHz, MeOD) δ 4.28 (d, *J* = 3.0 Hz, 1H, H-4), 4.25 (d, *J* = 13.5 Hz, 1H, H-6a), 4.02 – 3.98 (m, 1H, H-2), 3.99 (d, *J* = 12.5 Hz, 1H, H-6*a), 3.95 (t, *J* = 3.9 Hz, 1H, H-3), 3.90 (d, *J* = 11.8 Hz, 1H, H-6*b), 3.90 (d, *J* = 13.7 Hz, 1H, H-6b), 3.77 (d, *J* = 12.9 Hz, 1H, H-1a), 3.62 (dt, *J* = 17.4, 8.1 Hz, 1H, H-1'a), 3.53 – 3.44 (m, 1H, H-1b), 3.42 (t, *J* = 6.1 Hz, 1H, H-5'), 3.28 – 3.16 (m, 1H, H-1'b), 2.98 (s, 2H, H_2-6'), 1.95 (t, *J* = 3.0 Hz, 3H, 3 x CH ada), 1.90 – 1.80 (m, 1H, H-2'a), 1.82 – 1.65 (m, 6H, 3 x CH_2 ada), 1.72 – 1.61 (m, 1H, H-2'b), 1.68 – 1.61 (m, 2H, H_2-4'), 1.57 (d, *J* = 2.8 Hz, 6H, 3 x CH_2 ada), 1.55 – 1.39 (m, 2H, H_2-3'). ^{13}C NMR (100 MHz, MeOD) δ 81.7 (C-6'), 72.6 (C-5), 70.7 (C-5'), 69.2 (C-3), 65.4 (C-2), 64.1 (C-4), 55.8 (C-6*), 55.4 (C-6), 50.9 (C-1'), 47.7 (C-1), 39.4 (CH_2 ada), 36.9 (CH_2 ada), 33.7 (C_q ada), 28.7 (C-4'), 28.3 (CH ada), 25.3 (C-2'), 22.7 (C-3'). $[\alpha]^{20}_D$ = +0.2 (c = 0.73,

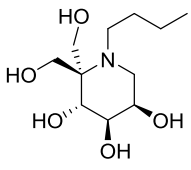
MeOH). IR/cm^{-1}: 3248, 2902, 2848, 1674, 1447, 1361, 1319, 1199, 1139, 1084, 1011. HRMS: found 428.30025 $[C_{23}H_{41}NO_6+H]^+$, calculated for $[C_{23}H_{41}NO_6+H]^+$ 428.30066.

5-*C*-Hydroxymethyl-*N*-[(biphenyl-4-yl-methoxy)-pentyl]-1-deoxy-D-galactonojirimycin (83):



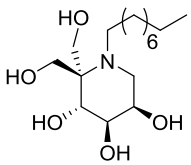
7 (0.20 mmol) and (biphenyl-4-yl-methoxy)pentyl bromide (0.30 mmol) was subjected to general alkylation procedure to provide **83** (18.6 mg, 0.04 mmol, yield 20%). ^{1}H NMR (400 MHz, MeOD) δ 7.68 – 7.60 (m, 4H, H_{Ar} BiPh), 7.52 – 7.41 (m, 4H, H_{Ar} BiPh), 7.39 – 7.32 (m, 1H, H_{Ar} BiPh), 4.57 (s, 2H, H_2-6'), 4.31 (d, *J* = 3.3 Hz, 1H, H-4), 4.26 (d, *J* = 14.0 Hz, 1H, H-6a), 4.02 – 3.99 (m, 1H, H-2), 4.00 (d, *J* = 11.7 Hz, 1H, H-6*a), 3.98 – 3.95 (m, 1H, H-3), 3.92 (d, *J* = 11.9 Hz, 1H, H-6*b), 3.91 (d, *J* = 14.1 Hz, 1H, H-6b), 3.76 (d, *J* = 13.0 Hz, 1H, H-1a), 3.69 – 3.61 (m, 1H, H-1'a), 3.58 (t, *J* = 6.1 Hz, 2H, H_2-5'), 3.41 (dd, *J* = 13.0, 3.4 Hz, 1H, H-1b), 3.28 – 3.20 (m, 1H, H-1'b), 1.99 – 1.84 (m, 1H, H-2'a), 1.83 – 1.75 (m, 1H, H-2'b), 1.73 (dt, *J* = 7.9, 6.1 Hz, 2H, H_2-4'), 1.65 – 1.43 (m, 2H, H_2-3'). ^{13}C NMR (100 MHz, MeOD) δ 132.0 – 128.6 (C_{Ar} BiPh), 74.9 (C-5), 74.5 (C-6'), 71.7 (C-5'), 71.4 (C-3), 68.0 (C-2), 66.4 (C-4), 58.1 (C-6*), 57.7 (C-6), 53.1 (C-1'), 50.8 (C-1), 30.9 (C-4'), 27.4 (C-2'), 24.9 (C-3'). $[\alpha]^{20}_D$ = +0.8 (c = 0.37, MeOH). IR/cm^{-1}: 3675, 3313, 2971, 1671, 1407, 1278, 1200, 1077, 1132. HRMS: found 446.25342 $[C_{25}H_{35}NO_6+H]^+$, calculated for $[C_{25}H_{35}NO_6+H]^+$ 446.25371.

5-*C*-Hydroxymethyl-*N*-butyl-1-deoxy-D-mannonojirimycin (98):



8 (0.20 mmol) and butyl bromide (0.30 mmol) was subjected to general alkylation procedure to provide **98** (12.6 mg, 0.05 mmol, yield 25%). ^{1}H NMR (400 MHz, MeOD) δ 4.16 (td, *J* = 3.6, 1.2 Hz, 1H, H-2), 4.15 (d, *J* = 10 Hz, 1H, H-4) 4.06 (d, *J* = 13.2 Hz, 1H, H-6a), 4.04 (dd, *J* = 9.6, 3.0 Hz, 1H, H-3), 3.92 (dd, *J* = 12.8, 0.8 Hz, 1H, H-1a), 3.90 (d, *J* = 13.2 Hz, 1H, H-6b), 3.87 (d, *J* = 12 Hz, 1H, H-6*a), 3.73 (d, *J* = 11.7 Hz, 1H, H-6*b), 3.61 (dd, *J* = 12.8, 3.6 Hz, 1H, H-1b), 3.60 – 3.53 (m, 1H, H-1'a), 3.23 (ddd, *J* = 13.3, 9.7, 4.6 Hz, 1H, H-1'b), 1.96 – 1.82 (m, 1H, H-2'a), 1.74 (m, 1H, H-2'b), 1.52 – 1.44 (m, 2H, H_2-3'), 1.05 (t, *J* = 7.3 Hz, 3H, H_3-4'). ^{13}C NMR (100 MHz, MeOD) δ 74.7 (C-5), 72.0 (C-3), 69.4 (C-4), 67.9 (C-2), 58.4 (C-6*), 58.1 (C-6), 55.1 (C-1), 52.6 (C-1'), 29.6 (C-2'), 21.3 (C-3'), 14.8 (C-4'). $[\alpha]^{20}_D$ = -19.8 (c = 0.25, MeOH). IR/cm^{-1}: 3675, 3325, 2970, 1393, 1250, 1057. HRMS: found 250.16490 $[C_{11}H_{23}NO_5+H]^+$, calculated for $[C_{11}H_{23}NO_5+H]^+$ 250.16490

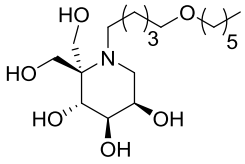
5-*C*-Hydroxymethyl-*N*-nonyl-1-deoxy-D-mannonojirimycin (99):



8 (0.20 mmol) and nonyl bromide (0.30 mmol) was subjected to general alkylation procedure to provide **99** (16.3 mg, 0.052 mmol, yield 26%). ^{1}H NMR (400 MHz, MeOD) δ 4.14 (d, *J* = 9.6 Hz, 1H, H-4), 4.13 (d, *J* = 3.6 Hz, 1H, H-2), 4.05 (d, *J* = 13.2 Hz, 1H, H-6a), 4.04 (dd, *J* = 9.6, 3.2 Hz, 1H, H-3), 3.90 (d, *J* = 13.2 Hz, 1H, H-1a), 3.88 (d, *J* = 13.2 Hz, 1H, H-6b), 3.87 (d, *J* = 12 Hz, 1H, H-6*a), 3.72 (d, *J* = 11.7 Hz, 1H, H-6*b), 3.59 (dd, *J* = 13.2, 3.6 Hz, 1H, H-1b), 3.58 – 3.52 (m, 1H, H-1'a), 3.27 – 3.16 (m, 1H, 1'b), 1.95 – 1.84 (m, 1H, H-2'a), 1.80 – 1.70 (m, 1H, H-2'b), 1.53 – 1.23 (m, 12H, H_2-3' – H_2-8'), 0.90 (t, *J* = 7.0 Hz, 3H, H_3-9'). ^{13}C NMR (100 MHz, MeOD) δ 72.4 (C-5), 69.7 (C-3), 67.1 (C-4), 65.7 (C-2), 56.2 (C-6), 55.8 (C-6*), 52.8 (C-1), 50.5 (C-1'), 31.6, 29.1, 28.9, 28.8, 25.7, 25.3, 22.3 (C-2' – C-8'), 13.0 (C-9'). $[\alpha]^{20}_D$ = -15.9 (c = 0.33, MeOH). IR/cm^{-1}: 3352, 2928, 2859, 1670, 1435, 1200, 1134, 1038. HRMS: found 320.24306 $[C_{16}H_{33}NO_5+H]^+$, calculated for $[C_{16}H_{33}NO_5+H]^+$ 320.24315.

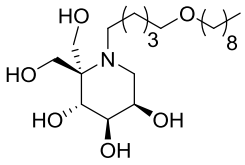
5-*C*-Hydroxymethyl-*N*-hexylpentyl-1-deoxy-D-mannonojirimycin (100):

8 (0.20 mmol) and pentyloxyhexyl bromide (0.31 mmol) was subjected to general alkylation procedure to provide **100** (14.0 mg, 0.038 mmol, yield 19%). ^{1}H NMR (400 MHz, MeOD) δ 4.14



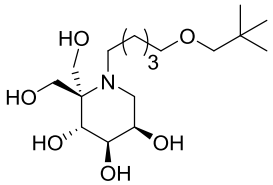
(d, *J* = 9,6 Hz, 1H, H-4), 4.14 (d, *J* = 4.0 Hz, 1H, H-2), 4.05 (d, *J* = 13.2 Hz, 1H, H-6a), 4.04 (dd, *J* = 9.6, 3.0 Hz, 1H, H-3), 3.91 (d, *J* = 12 Hz, 1H, H-1a), 3.89 (d, *J* = 13.2 Hz, 1H, H-6b), 3.87 (d, *J* = 12 Hz, 1H, H-6*a), 3.72 (d, *J* = 11.7 Hz, 1H, H-6*b), 3.60 (dd, *J* = 12.8, 3.2 Hz, 1H, H-1b), 3.60 – 3.51 (m, 1H, H-1'a), 3.48 (t, *J* = 6.2 Hz, 2H, H_2-5'), 3.45 (t, *J* = 6.6 Hz, 2H, H_2-6'), 3.26 – 3.19 (m, 1H, H-1'b), 2.01 – 1.72 (m, 2H, H_2-2'), 1.72 – 1.63 (m, 2H, H_2-4'), 1.63 – 1.53 (m, 2H, H_2-7'), 1.56 – 1.44 (m, 2H, H_2-3'), 1.43 – 1.29 (m, 6H, H_2-8', H_2-9', H_2-10'), 0.93 (t, *J* = 6.7 Hz, 3H, H_3-11'). ^{13}C NMR (100 MHz, MeOD) δ 72.4 (C-5), 70.7 (C-6'), 69.9 (C-5'), 69.7 (C-3), 67.1 (C-4), 65.7 (C-2), 56.2 (C-6*), 55.8 (C-6), 52.9 (C-1), 50.4 (C-1'), 31.5 (C-9'), 29.4 (C-7'), 28.7 (C-4'), 25.6 (C-8'), 25.1 (C-2'), 22.6 (C-3'), 22.3 (C-10'), 13.0 (C-11'). $[\alpha]^{20}_D$ = -15.0 (c = 0.28, MeOH). IR/cm^{-1}: 3327, 2930, 2860, 1672, 1464, 1431, 1377, 1202, 1134, 1040. HRMS: found 364.27001 $[C_{18}H_{37}NO_6+H]^+$, calculated for $[C_{18}H_{37}NO_6+H]^+$ 364.26936.

5-*C*-Hydroxymethyl-*N*-nonylpentyl-1-deoxy-D-mannonojirimycin (101):



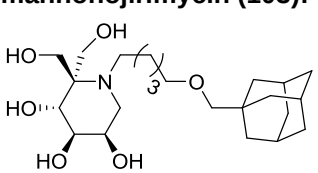
8 (0.20 mmol) pentyloxynonyl bromide (0.30 mmol) was subjected to general alkylation procedure to provide **101** (14.2 mg, 0.034 mmol, yield 17%). ^{1}H NMR (400 MHz, MeOD) δ 3.98 (d, *J* = 9.9 Hz, 1H, H-4), 3.97 (d, *J* = 4.0 Hz, 1H, H-2), 3.93 – 3.87 (m, 1H, H-3), 3.91 (d, *J* = 12.5 Hz, 1H, H-6a), 3.86 (d, *J* = 12.4 Hz, 1H, H-6b), 3.84 (d, *J* = 11.4 Hz, 1H, H-6*a), 3.72 (d, *J* = 11.3 Hz, 1H, H-6*b), 3.47 (t, *J* = 6.6 Hz, 2H, H_2-5'), 3.45 (t, *J* = 6.7 Hz, 2H, H_2-6'), 3.53 – 3.42 (m, 1H, H-1a), 3.28 – 3.12 (m, 2H, H-1b, H-1'a), 2.82 – 2.58 (m, 1H, H-1'b), 1.78 – 1.53 (m, 6H, H_2-2', H_2-4', H_2-7'), 1.51 – 1.20 (m, 14H, H_2-3', H_2-8', H_2-9', H_2-10', H_2-11', H_2-12', H_2-13'), 0.91 (t, *J* = 6.9 Hz, 3H, H_3-14'). ^{13}C NMR (100 MHz, MeOD) δ 72.9 (C-6'),72.8 (C-5), 72.5 (C-5'), 70.8 (C-3), 68.9 (C-2), 67.5 (C-4), 53.7 (C-1), 51.6 (C-1'), 33.9 (C-9'), 31.7, 31.6, 31.6, 31.5, 31.4, 31.3, 28.1, 25.5, 24.6 (C-2', C-3', C-4', C-7', C-8', C-10', C-11', C-12', C-13'), 15.3 (C-14'). $[\alpha]^{20}_D$ = -15.5 (c = 0.28, MeOH). IR/cm^{-1}: 3357, 2928, 1738, 1676, 1438, 1365, 1216, 1137. HRMS: found 406.31603 $[C_{21}H_{43}NO_6+H]^+$, calculated for $[C_{21}H_{43}NO_6+H]^+$ 406.31631.

5-*C*-Hydroxymethyl-*N*-[5-(3,3-dimethyl-1-propyloxy)pentyl]-1-deoxy-D-mannonojirimycin (102):



8 (0.20 mmol) and 1-bromo-5-(2,2-dimethyl-1-propoxy)pentane (0.30 mmol) was subjected to general alkylation procedure to provide **102** (11.7 mg, 0.034 mmol, yield 17%). ^{1}H NMR (400 MHz, MeOD) δ 4.14 (d, *J* = 9.6 Hz, 1H, H-4), 4.14 (dd, *J* = 3.1, 1.1 Hz, 1H, H-2), 4.05 (d, *J* = 13.6 Hz, 1H, H-6a), 4.04 (dd, *J* = 9.9, 3.1 Hz, 1H, H-3), 3.92 (d, *J* = 12.8 Hz, 1H, H-1b), 3.89 (d, *J* = 13.2 Hz, 1H, H-6b), 3.87 (d, *J* = 11.2 Hz, 1H, H-6*a), 3.72 (d, *J* = 11.7 Hz, 1H, H-6*b), 3.61 (dd, *J* = 12.6, 3.5 Hz, 1H, H-1a), 3.58 – 3.53 (m, 2H, H_2-1'a), 3.48 (t, *J* = 6.1 Hz, 2H, H_2-5'), 3.29 – 3.19 (m, 1H, H-1'b), 3.11 (s, 2H, H_2-6'), 1.94 (m, 1H, H-2'a), 1.87 – 1.73 (m, 1H, H-2'b), 1.73 – 1.64 (m, 2H, H_2-3'), 1.54 (m , 2H, H_2-4'), 0.94 (s, 9H, 3 x CH_3). ^{13}C NMR (100 MHz, MeOD) δ 83.4 (C-6'), 73.5 (C-5),)72.9 (C-5'), 72.0 (C-3), 69.4 (C-4), 67.9 (C-2), 58.4, 58.1 (C-6, C-6*), 55.1 (C-1), 52.7 (C-1'), 33.8 (C-7') 31.1 (C-3'), 28.0 (3 x CH_3), 27.4 (C-2'), 25.0 (C-4'). $[\alpha]^{20}_D$ = -15.4 (c = 0.23, MeOH). IR/cm^{-1}: 3675, 2988, 2901, 1674, 1393, 1250, 1066. HRMS: found 350.25352 $[C_{17}H_{35}NO_6+H]^+$, calculated for $[C_{17}H_{35}NO_6+H]^+$ 350.25371.

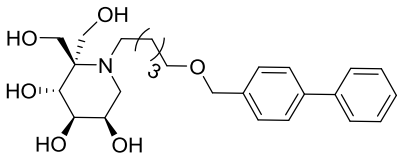
5-*C*-Hydroxymethyl-*N*-[5-(adamantan-1-yl-methoxy)-pentyl]-1-deoxy-D-mannonojirimycin (103):



8 (0.20 mmol) and 5-(adamantan-1-yl-methoxy)pentyl bromide (0.30 mmol) was subjected to general alkylation procedure to provide **103** (10.5 mg, 0.024 mmol, yield 12%). ^{1}H NMR (400 MHz, MeOD) δ 4.14 (d, *J* = 9.6, 1H, H-4), 4.15 – 4.14 (m, 1H, H-2), 4.06 (d, *J* = 13.2, 1H, H-6a), 4.04 (dd, *J* = 9.6, 2.8, 1H, H-3), 3.92

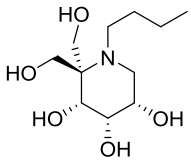
(dd, *J* = 13.2, 1.2, 1H, H-1b), 3.89 (d, *J* = 13.6, 1H, H-6b), 3.88 (d, *J* = 11.6, 1H, H-6*a), 3.73 (d, *J* = 11.7, 1H, H-6*b), 3.61 (dd, *J* = 12.9, 3.4 Hz, 1H, H-1a), 3.62 – 3.52 (m, 1H, H-1'a), 3.45 (t, *J* = 6.1 Hz, 2H, H_2-5'), 3.23 (ddd, *J* = 13.4, 9.9, 4.6 Hz, 1H, H-1'b), 1.98 (br s, 3H, CH ada), 1.96 – 1.89 (m, 1H, H-2'a), 1.85 – 1.75 (m, 1H, H-2'b), 1.83 – 1.68 (m, 6H, 3 x CH_2 ada), 1.70 – 1.63 (m, 2H, H_2-4'), 1.59 (d, *J* = 2.8 Hz, 6H, 3 x CH_2 ada), 1.57 – 1.48 (m, 2H, H_2-3'). ^{13}C NMR (100 MHz, MeOD) δ 84.0 (C-6'), 74.7 (C-5), 73.0 (C-5'), 72.0 (C-3), 69.4 (C-4), 67.9 (C-2), 58.4 (C-6*), 58.1 (C-6), 53.8 (C-1), 52.7 (C-1'), 41.7 (CH_2 ada), 39.2 (CH_2 ada), 36.0 (C_q ada), 31.0 (C-4'), 30.6 (CH ada), 27.5 (C-2'), 25.0 (C-3'). $[\alpha]^{20}_D$ = -13.3 (c = 0.21, MeOH). IR/cm^{-1}: 3675, 3330, 2901, 1673, 1450, 1203, 1134, 1077. HRMS: found 428.2999 $[C_{23}H_{41}NO_6+H]^+$, calculated for $[C_{23}H_{41}NO_6+H]^+$ 428.30066.

5-*C*-Hydroxymethyl-*N*-[(biphenyl-4-yl-methoxy)-pentyl]-1-deoxy-D-mannonojirimycin (104):



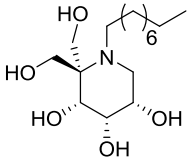
8 (0.20 mmol) and (biphenyl-4-yl-methoxy)pentyl bromide (0.32 mmol) was subjected to general alkylation procedure to provide **104** (17.1 mg, 0.038 mmol, yield 19%). ^{1}H NMR (400 MHz, MeOD) δ 7.64 (m, 4H, H_{Ar} BiPh), 7.50 – 7.40 (m, 4H, H_{Ar} BiPh), 7.40 – 7.29 (m, 1H, H_{Ar} BiPh), 4.58 (s, 2H, H_2-6'), 4.14 (d, *J* = 9.8 Hz, 1H, H-4), 4.15 - 4.11 (t, *J* = 3.2 Hz, 1H, H-2), 4.04 (d, *J* = 13.2, 1H, H-6a), 4.03 (dd, *J* = 10.0, 2.8, 1H, H-3), 3.89 (d, *J* = 13.2, 1H, H-6b), 3.87 (d, *J* = 12.0, 1H, H-6*a), 3.87 (m, 1H, H-1a) 3.71 (d, *J* = 11.6, 1H, H-6*b), 3.65 – 3.54 (m, 1H, H-1'a), 3.59 (t, *J* = 5.8 Hz, 2H, H_2-5'), 3.64 - 3.55 (m, 1H, H-1b), 3.28 – 3.17 (m, 1H, H-1'b), 2.01 – 1.86 (m, 1H, H-2'a), 1.86 – 1.77 (m, 1H, H-2'b), 1.78 – 1.70 (m, 2H, H-4'), 1.68 – 1.46 (m, 2H, H-3'). ^{13}C NMR (100 MHz, MeOD) δ 140.5, 137.5 (C_q BiPh), 129.7, 128.7, 128.5, 128.1, 127.0, 126.6, 126.5 (C_{Ar} BiPh), 72.4 (C-5), 72.2 (C-6'), 69.7 (C-3), 69.5 (C-5'), 67.1 (C-4), 65.7 (C-2), 56.2 (C-6*), 55.8 (C-6), 52.8 (C-1), 50.4 (C-1'), 28.7 (C-2'), 25.0 (C-3'), 22.7 (C-4'). $[\alpha]^{20}_D$ = -14.6 (c = 0.34, MeOH). IR/cm^{-1}: 3675, 3323, 2971, 1674, 1407, 1202, 1133, 1076. HRMS: found 446.25345 $[C_{25}H_{35}NO_6+H]^+$, calculated for $[C_{25}H_{35}NO_6+H]^+$ 446.25371.

5-*C*-Hydroxymethyl-*N*-butyl-1-deoxy-D-allonojirimycin (121):



9 (0.20 mmol) and butyl bromide (0.30 mmol) was subjected to general alkylation procedure to provide **121** (6.2 mg, 0.025 mmol, yield 12%). ^{1}H NMR (600 MHz, MeOD) δ 4.18 (d, *J* = 14.2 Hz, 1H, H-6a), 4.08 (t, *J* = 2.9 Hz, 1H, H-3), 3.97 (d, *J* = 12.1 Hz, 1H, H-6*a), 3.94 – 3.90 (m, 1H, H-2), 3.89 (d, *J* = 12.6 Hz, 1H, H-6*b), 3.89 (d, *J* = 2.7 Hz, 1H, H-4), 3.87 (d, *J* = 14.2 Hz, 1H, H-6b), 3.61 (ddd, *J* = 13.0, 11.9, 5.0 Hz, 1H, H-1'), 3.36 – 3.34 (m, 2H, H_2-1), 1.92 – 1.80 (m, 1H, H-2'a), 1.76 – 1.59 (m, 1H, H-2'b), 1.54 – 1.33 (m, 2H, H_2-3'), 1.01 (t, *J* = 7.4 Hz, 3H, H_3-4'). ^{13}C NMR (150 MHz, MeOD) δ 72.6 (C-5), 71.8 (C-3), 67.5 (C-4), 65.1 (C-2), 57.0 (C-6), 57.0 (C-6*), 53.0 (C-1'), 49.0 (C-1), 28.4 (C-2'), 21.1 (C-3'), 13.9 (C-4'). $[\alpha]^{20}_D$ = -0.2 (c = 0.12, MeOH). IR/cm^{-1}: 3352, 2970, 2879, 1674, 1430, 1201, 1136, 1056. HRMS: found 250.16502 $[C_{11}H_{23}NO_5+H]^+$, calculated for $[C_{11}H_{23}NO_5+H]^+$ 250.16490.

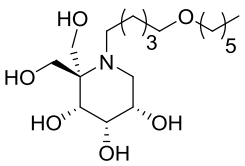
5-*C*-Hydroxymethyl-*N*-nonyl-1-deoxy-D-allonojirimycin (122):



9 (0.20 mmol) and nonyl bromide (0.30 mmol) was subjected to general alkylation procedure with to provide **122** (8.3 mg, 0.026 mmol, yield 13%). ^{1}H NMR (400 MHz, MeOD) δ 4.21 (d, *J* = 14.3 Hz, 1H, H-6a), 4.10 (t, *J* = 2.9 Hz, 1H, H-3), 3.99 (d, *J* = 12.1 Hz, 1H, H-6*a), 3.95 (dd, *J* = 6.5, 3.1 Hz, 1H, H-2), 3.92 (d, *J* = 12.4 Hz, 1H, H-6*b), 3.91 (d, *J* = 2.4 Hz, 1H, H-4), 3.89 (d, *J* = 14 Hz, 1H, H-6b), 3.63 (td, *J* = 12.4, 5.0 Hz, 1H, H-1'a), 3.42 – 3.35 (m, 2H, H_2-1), 3.14 (dt, *J* = 12.5, 6.3 Hz, 1H, H-1'b), 1.98 – 1.66 (m, 2H, H_2-2'), 1.46 – 1.33 (m, 12H, H_2-3' - H_2-8'), 0.94 (t, *J* = 7.1 Hz, 3H, H_3-9'). ^{13}C NMR (100 MHz, MeOD) δ 71.2 (C-5), 70.3 (C-3), 66.1 (C-4), 63.7 (C-2), 55.6 (C-6), 55.6 (C-6*), 51.8 (C-1'), 47.5 (C-1), 31.6, 29.1, 28.9, 28.8, 26.4, 25.0, 22.3 (C-2' - C-8'), 13.0 (C-9'). $[\alpha]^{20}_D$ = -0.2 (c = 0.17, MeOH). IR/cm^{-1}: 3352, 2926, 2858, 1670, 1456, 1435, 1379,

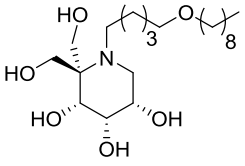
1201, 1134, 1056. HRMS: found 320.24328 $[C_{16}H_{33}NO_5+H]^+$, calculated for $[C_{16}H_{33}NO_5+H]^+$ 320.24315.

5-*C*-Hydroxymethyl-*N*-hexyloxypentyl-1-deoxy-D-allonojirimycin (123):



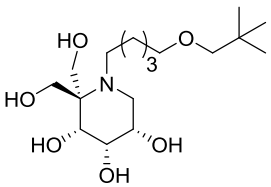
9 (0.20 mmol) and pentyloxyhexyl bromide (0.30 mmol) was subjected to general alkylation procedure to provide **123** (5.0 mg, 0.014 mmol, yield 7%). ^{1}H NMR (600 MHz, MeOD) δ 4.21 (d, *J* = 14.2 Hz, 1H, H-6a), 4.10 (t, *J* = 2.8 Hz, 1H, H-3), 3.99 (d, *J* = 12.1 Hz, 1H, H-6*a), 3.96 – 3.93 (m, 2H, H_2-2), 3.91 (d, *J* = 12.4 Hz, 1H, H-6*b), 3.91 (d, *J* = 2.7 Hz, 1H, H-4), 3.89 (d, *J* = 14.3 Hz, 1H, H-6b), 3.68 – 3.59 (m, 1H, H-1'a), 3.48 (t, *J* = 6.3 Hz, 2H, H_2-5'), 3.46 (t, *J* = 6.6 Hz, 2H, H_2-6'), 3.40 – 3.36 (m, 2H, H_2-1), 3.15 (td, *J* = 12.4, 5.0 Hz, 1H, H-1'b), 1.96 – 1.90 (m, 1H, H-2'a), 1.80 – 1.71 (m, 1H, H-2'b), 1.68 – 1.66 (m, 2H, H_2-4'), 1.60 – 1.56 (m, 2H, H_2-7'), 1.55 – 1.44 (m, 2H, H_2-3'), 1.42 – 1.30 (m, 6H, H_2-8', H_2-9', H_2-10'), 0.93 (t, *J* = 6.9 Hz, 3H, H_3-11'). ^{13}C NMR (150 MHz, MeOD) δ 72.3 (C-5), 71.7 (C-6'), 71.4 (C-3), 71.0 (C-5'), 67.1 (C-4), 64.7 (C-2), 56.6 (C-6), 56.6 (C-6*), 52.7 (C-1'), 48.5 (C-1), 31.9 (C-9'), 30.3 (C-7'), 29.8 (C-4'), 26.6 (C-8'), 25.8 (C-2'), 24.2 (C-3'), 23.3 (C-10'), 14.0 (C-11'). $[\alpha]^{20}_D$ = +0.0 (c = 0.10, MeOH). IR/cm^{-1}: 3352, 2929, 2860, 1751, 1676, 1431, 1371, 1205, 1132, 1080. HRMS: found 264.26942 $[C_{18}H_{37}NO_6+H]^+$, calculated for $[C_{18}H_{37}NO_6+H]^+$ 264.26936.

5-*C*-Hydroxymethyl-*N*-nonyloxypentyl-1-deoxy-D-allonojirimycin (124):



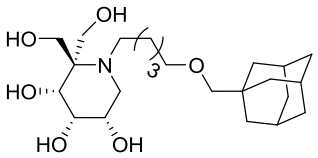
9 (0.20 mmol) and pentyloxynonyl bromide (0.30 mmol) was subjected to general alkylation procedure to provide **124** (3.3 mg, 0.008 mmol, yield 4%). ^{1}H NMR (600 MHz, MeOD) δ 4.21 (d, *J* = 14.3 Hz, 1H, H-6a), 4.10 (t, *J* = 2.9 Hz, 1H, H-3), 3.99 (d, *J* = 12.1 Hz, 1H, H-6*a), 3.96 – 3.93 (m, 1H, H-2), 3.91 (d, *J* = 12 Hz, 1H, H-6*b), 3.91 (d, *J* = 2.4 Hz, 1H, H-4), 3.89 (d, *J* = 14.4 Hz, 1H, H-6b), 3.67 – 3.60 (m, 1H, H-1'a), 3.48 (t, *J* = 6.3 Hz, 2H, H_2-5'), 3.46 (t, *J* = 6.6 Hz, 2H, H_2-6'), 3.39 – 3.33 (m, 2H, H_2-1), 3.15 (td, *J* = 12.5, 5.0 Hz, 1H, H-1'b), 1.99 – 1.88 (m, 1H, H-2'a), 1.84 – 1.72 (m, 1H, H-2'b), 1.68 – 1.66 (m, 2H, H_2-4'), 1.58 (dt, *J* = 8.0, 6.4 Hz, 2H, H_2-7'), 1.55 – 1.45 (m, 2H, H_2-3'), 1.41 – 1.27 (m, 12H, H_2-8' – H_2-13'), 0.93 (t, *J* = 7.1 Hz, 3H, H_3-14'). ^{13}C NMR (150 MHz, MeOD) δ 72.3 (C-5), 71.7 (C-6'), 71.4 (C-3), 71.0 (C-5'), 67.1 (C-4), 64.7 (C-2), 56.6 (C-6), 56.6 (C-6*), 52.7 (C-1'), 49.5 (C-1), 32.7 (C-9'), 30.4 (C-7'), 30.3, 30.2, 30.0 (C-10', C-11', C-12'), 29.8 (C-4'), 26.9 (C-8'), 25.8 (C-2'), 24.2 (C-3'), 23.3 (C-13'), 14.1 (C-14'). $[\alpha]^{20}_D$ = -0.2 (c = 0.07, MeOH). IR/cm^{-1}: 3292, 2924, 2856, 1676, 1425, 1205, 1134, 1055. HRMS: found 406.31623 $[C_{21}H_{43}NO_6+H]^+$, calculated for $[C_{21}H_{43}NO_6+H]^+$ 406.31631.

5-*C*-Hydroxymethyl-*N*-[5-(3,3-dimethyl-1-propyloxy)pentyl]-1-deoxy-D-allonojirimycin (125):



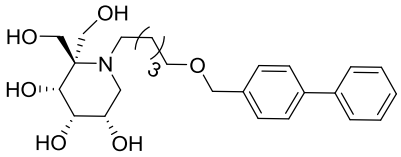
9 (0.20 mmol) and 1-bromo-5-(2,2-dimethyl-1-propoxy)pentane (0.31 mmol) was subjected to general alkylation procedure with to provide **125** (13.8 mg, 0.04 mmol, yield 20%). ^{1}H NMR (400 MHz, MeOD) δ 4.21 (d, *J* = 14.3 Hz, 1H, H-6a), 4.11 (t, *J* = 2.9 Hz, 1H, H-3), 4.00 (d, *J* = 12.1 Hz, 1H, H-6*a), 3.98 – 3.94 (m, 1H. H-2), 3.92 (d, *J* = 12.4 Hz, 1H, H-6*b), 3.92 (d, *J* = 3.2 Hz, 1H, H-4), 3.90 (d, *J* = 14.8 Hz, 1H, H-6b), 3.65 (td, *J* = 12.4, 5.0 Hz, 1H, H-1'a), 3.47 (t, *J* = 6.2 Hz, 2H, H_2-5'), 3.42 – 3.38 (m, 2H, H_2-1), 3.22 – 3.13 (m, 1H, H-1'b), 3.10 (s, 2H, H_2-6'), 2.01 – 1.89 (m, 1H, H-2'a), 1.88 – 1.73 (m, 1H, H-2'b), 1.67 (dt, *J* = 7.9, 6.4 Hz, 2H, H_2-4'), 1.58 – 1.48 (m, 2H, H_2-3'), 0.93 (s, 9H, 3 x CH_3). ^{13}C NMR (100 MHz, MeOD) δ 81.1 (C-6'), 71.3 (C-5), 70.6 (C-5'), 70.3 (C-3), 66.2 (C-4), 63.7 (C-2), 55.7, 55.7 (C-6, C-6*), 51.7 (C-1'), 47.2 (C-1), 31.5 (C-7'), 28.9 (C-4'), 25.8 (CH_3), 24.8 (C-2'), 23.3 (C-3'). $[\alpha]^{20}_D$ = -0.3 (c = 0.28, MeOH). IR/cm^{-1}: 3675, 2971, 1672, 1393, 1202, 1066. HRMS: found 350.25347 $[C_{17}H_{35}NO_6+H]^+$, calculated for $[C_{17}H_{35}NO_6+H]^+$ 350.25371.

5-*C*-Hydroxymethyl-*N*-[5-(adamantan-1-yl-methoxy)-pentyl]-1-deoxy-D-allonojirimycin (126):



9 (0.20 mmol) and 5-(adamantan-1-yl-methoxy)pentyl bromide (0.29 mmol) was subjected to general alkylation procedure to provide **126** (9.5 mg, 0.022 mmol, yield 11%). ^{1}H NMR (400 MHz, MeOD) δ 4.21 (d, *J* = 14.2 Hz, 1H, H-6a), 4.10 (t, *J* = 2.9 Hz, 1H, H-3), 3.98 (d, *J* = 12.4 Hz, 1H, H-6*a), 3.96 – 3.92 (m, 1H, H_2-2), 3.91 (d, *J* = 12.4 Hz, 1H, H-6*b), 3.91 (d, *J* = 2.8 Hz, 1H, H-4), 3.90 (d, *J* = 14 Hz, 1H, H-6b), 3.64 (td, *J* = 12.3, 4.9 Hz, 1H, H-1'a), 3.44 (t, *J* = 6.2 Hz, 2H, H_2-5'), 3.41 – 3.35 (m, 2H, H_2-1), 3.22 – 3.10 (m, 1H, H-1'b), 1.97 (t, *J* = 3.2 Hz, 3H, 3 x CH ada), 1.97 – 1.90 (m, 1H, H_2-2'a), 1.80 – 1.68 (m, 6H, 3 x CH_2 ada), 1.74 – 1.69 (m, 1H, H-2'b), 1.70 – 1.62 (m, 2H, H_2-4'), 1.59 (d, *J* = 2.9 Hz, 6H, 3 x CH_2 ada), 1.56 – 1.44 (m, 2H, H-3'). ^{13}C NMR (100 MHz, MeOD) δ 81.7 (C-6'), 71.3 (C-5), 70.7 (C-5'), 70.3 (C-3), 66.1 (C-4), 63.7 (C-2), 55.6 (C-6), 55.6 (C-6*) 51.7 (C-1'), 48.3 (C-1), 39.4 (CH_2 ada), 36.9 (CH_2 ada), 33.8 (C_q ada), 28.8 (C-4'), 28.3 (CH ada), 24.8 (C-2'), 23.3 (C-3'). $[\alpha]^{20}_{D}$ = -0.1 (c = 0.19, MeOH). IR/cm^{-1}: 3675, 2988, 1673, 1394, 1205, 1131, 1066. HRMS: found 428.30043 $[C_{23}H_{41}NO_6+H]^+$, calculated for $[C_{23}H_{41}NO_6+H]^+$ 428.30066.

5-*C*-Hydroxymethyl-*N*-[(biphenyl-4-yl-methoxy)-pentyl]-1-deoxy-D-allonojirimycin (127):



9 (0.20 mmol) and (biphenyl-4-yl-methoxy)pentyl bromide (0.30 mmol) was subjected to general alkylation procedure to provide **127** (2.8 mg, 0.0062 mmol, yield 3%). ^{1}H NMR (600 MHz, MeOD) δ 7.65 – 7.57 (m, 4H, H_{Ar} BiPh), 7.43 (d, *J* = 8.0 Hz, 4H, H_{Ar} BiPh), 7.34 (d, *J* = 7.4 Hz, 1H, H_{Ar} BiPh), 4.56 (s, 2H, H-6'), 4.17 (d, *J* = 14.3 Hz, 1H, H-6a), 4.07 (t, *J* = 2.9 Hz, 1H, H-3), 3.96 (d, *J* = 12.2 Hz, 1H, H-6b), 3.92 – 3.89 (m, 1H, H-2), 3.90 (d, *J* = 14.4 Hz, 1H, H-6*a), 3.88 (d, *J* = 3 Hz, 1H, H-4), 3.86 (d, *J* = 13.8 Hz, 1H, H-6*b), 3.64 – 3.59 (m, 1H, H-1'a), 3.56 (t, *J* = 3.56, 2H, H_2-5'), 3.37 – 3.32 (m, 2H, H_2-1), 3.17 – 3.10 (m, 1H, H-1'b), 1.97 – 1.88 (m, 1H, H-2'a), 1.80 – 1.73 (m, 1H, H-2'b), 1.74 – 1.68 (m, 2H, H_2-4'), 1.59 – 1.46 (m, 2H, H_2-3'). ^{13}C NMR (150 MHz, MeOD) δ 142.1, 141.9 (C_q Bn), 138.8, 129.9, 129.4, 128.4, 128.0, 127.9 (C_{Ar} BiPh), 73.7 (C-6'), 71.8 (C-3), 71.0 (C-5'), 67.5 (C-4), 65.1 (C-2), 62.6 (C-5), 57.0 (C-6), 56.9 (C-6*), 53.1 (C-1'), 49.9 (C-1), 30.2 (C-4'), 26.2 (C-2'), 24.7 (C-3'). $[\alpha]^{20}_{D}$ = +0.54 (c = 0.06, MeOH). IR/cm^{-1}: 3337, 2928, 2863, 1738, 1673, 1442, 1365, 1205, 1130. HRMS: found $[C_{25}H_{35}NO_6+H]^+$ 446.25357, calculated for $[C_{25}H_{35}NO_6+H]^+$ 446.25371.

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