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

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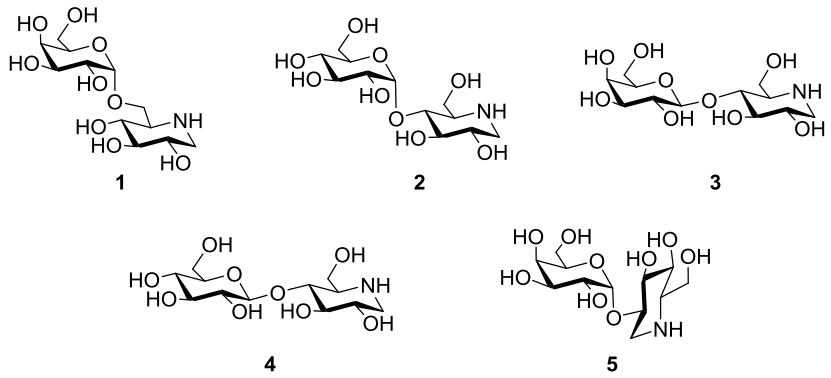
7 Summary, Work in Progress and Future Prospects

This Thesis describes the design, synthesis and evaluation as glycoprocessing enzyme inhibitors of focused libraries of iminosugars. In the studies described, 1-deoxynojirimycin (DNJ), the archetypal iminosugar, and its known *N*-alkylated derivatives, served as starting points. DNJ modifications presented here include alteration of the substitution pattern of the piperidine core structure; variation in the N substituent, or a combination of the two. Biological evaluation of the synthesized compounds focused on the glycoprocessing enzymes involved in glucosylceramide metabolism: glucosylceramide synthase (GCS), lysosomal glucosylceramidase (GBA1) and neutral glucosylceramidase (GBA2), and in all examples presented the inhibitory potency of newly synthesized compounds are compared with that of literature compounds.

In **Chapter 1** the current and potential applications of iminosugars in biomedicine are introduced. Given the importance of this class of compounds, numerous synthetic strategies have been reported over the decades, thus allowing the synthesis of natural compounds that are hard to access in large quantities and/or purity from nature, but also to expand the structural diversity. **Chapter 2** reviews some particularly versatile synthetic strategies for the construction of DNJ, including strategies involving a double reductive amination as a key step – a key step that also features in several routes of synthesis as presented in this Thesis.

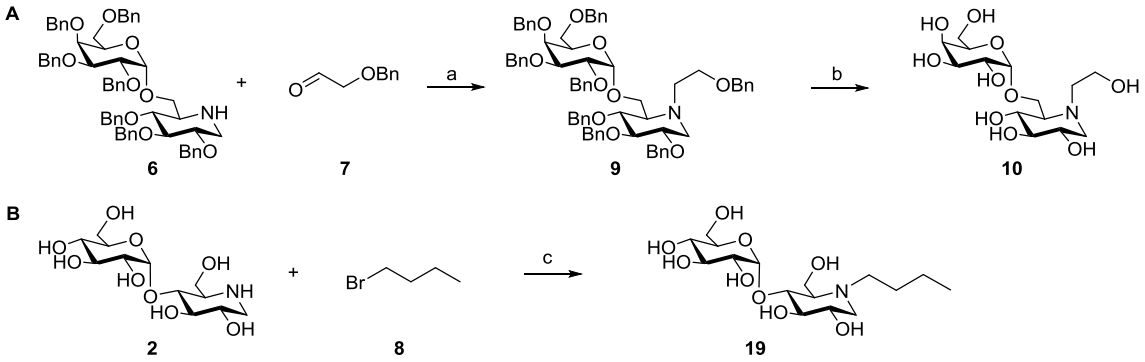
Glycosylated DNJs comprise a relatively less well explored class of iminosugars when compared to monosaccharidic DNJs. In **Chapter 3** an efficient method is described for the synthesis of glycosylated DNJ derivatives starting from the corresponding disaccharides. Five different glycosylated DNJ structures were successfully constructed (**1** – **5**, Figure 1) following a route comprising selective liberation of the anomeric center of the reducing glucose in the starting disaccharides followed by reduction to the diol, oxidation to the 5-keto aldehyde and double reductive amination.

***Figure 1**: Glycosylated 1-deoxynojirimycin (**1** - **5**) constructed in Chapter 3*



N-alkyl derivatives of some of these glycosylated iminosugars (see for the synthesized structures Table 1) were prepared as depicted in scheme 1. As an example, reductive amination of the per-*O*-benzyl protected iminodisaccharide **6** with sodium cyanoborohydride as the reducing agent and including the appropriate aldehyde provides, after global deprotection, hydroxyethyl derivative **10** (Scheme 1A; see for experimental details the experimental section at the end of this Chapter). Alternatively, fully deprotected iminodisaccharide **2** can be subjected to butyl bromide and potassium carbonate in DMF to yield *N*-butyl-iminodisaccharide **19** (Scheme 1B). A combination of both approaches should enable the synthesis of the complete panel as depicted in Table 1.

***Scheme 1**: N-Alkylation strategies of glycosylated DNJ derivatives (**9 - 28**)*



Reagents and conditions: [a] AcOH, $NaCHBH_3$, MeOH, DCM, 64%; [b] Pd/C, H_2, DMF/MeOH, 91%; [c] K_2CO_3, DMF, 85 °C, 58%.

***Table 1**: Code of the synthesized N-alkyl glycosylated DNJ derivatives*

	*Melibio DNJ (**1**)*	*Malto DNJ (**2**)*	*Lacto DNJ (**3**)*	*Cellobio DNJ (**4**)*
N-hydroxyethyl	[a] **9**, [b] **10**	N.S.	N.S.	N.S.
N-butyl	[a] **11**, [b] N.S.	[a] **18**, [b] **19**	N.S.	[c] **23**
N-nonyl	[a] **12**, [b] **13**	[a] **20**, [b] N.S.	N.S.	[c] **24**
N-5-(hexyloxy)pentyl	N.S.	N.S.	[c] **21**	[c] **25**
N-5-(nonyloxy)pentyl	[c] **14**	N.S.	N.S.	[c] **26**
N-(biphenyl-4-yl-methoxy)pentyl	[c] **15**	N.S.	N.S.	[c] **27**
N-5-(adamantan-1-yl-methoxy)pentyl	[c] **16**	N.S.	[c] **22**	N.S.
N-5-(3,3-dimethyl-1-propyloxy)pentyl	[c] **17**	N.S.	N.S.	[c] **28**

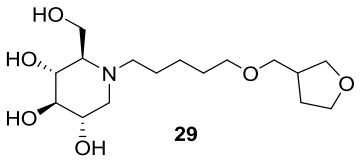
*N.S.: not synthesized or purified.

*[a],[b],[c]: synthesized via conditions a, b or c described in scheme 1.

GBA2 selective inhibitors are desirable commodities both for fundamental biological studies on the physiological role of GBA2 and as potential clinical candidates, in case GBA2 turns out to be a relevant drug target (as is currently considered in relation to the lysosomal storage disorders, Gaucher disease and Niemann-Pick type C disease). Unfortunately, all GBA2

inhibitors described in the literature have overlapping activities on either of the two other GlcCer metabolism relating enzymes, GCS and GBA1. **Chapter 4** discusses the design and synthesis of *N*-alkyl DNJ derivatives as potential GBA2 selective inhibitors. A focused library composed of *N*-pentyloxy neopentyl isosteres iminosugars was built and evaluated, and compound **29** (Figure 2) was found to be the most selective GBA2 inhibitor of the investigated series.

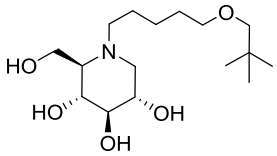
***Figure 2**: Most promising GBA2 selective inhibitor from Chapter 4*



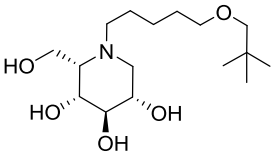
29

Studies on configurational iminosugars have revealed that D-*ido*-configured DNJ derivatives possess remarkable GBA2 selectivity. As depicted in Figure 3, D-*ido*-configured, *N*-alkyl derivative **32** is a low nanomolar GBA2 inhibitor. The compound is even more potent than the known GBA2 inhibitors **30** and **31**, and is also more selective (**32**: $IC_{50\ GCS}/IC_{50\ GBA2}$ 1750, $IC_{50\ GBA1}/IC_{50\ GBA2}$ 92071; **30**: $IC_{50\ GCS}/IC_{50\ GBA2}$ 1020, $IC_{50\ GBA1}/IC_{50\ GBA2}$ 1252).

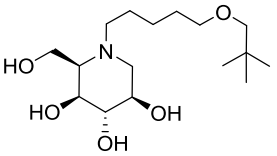
***Figure 3**: Structure and inhibitory activity of D-gluco, L-ido and D-ido iminosugars*



30, D-*gluco* NEO
IC_{50} GCS 5 μM
IC_{50} GBA1 6 μM
IC_{50} GBA2 5 nM



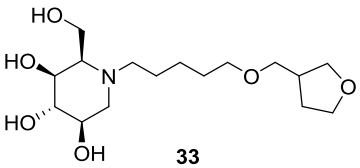
31, L-*ido* NEO
IC_{50} GCS 1.6 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 10 nM



32, D-*ido* NEO
IC_{50} GCS 7 μM
IC_{50} GBA1 387 μM
IC_{50} GBA2 4 nM

Hence, D-*ido* structural iminosugar is a promising starting point for further research on GBA2 selective inhibitors, for instance by variation of the *N*-alkyl substituent as has been the object of study in **Chapter 4** (leading to, for instance, compound **33**, Figure 4).

***Figure 4**: Structure of designed GBA2 selective inhibitor*



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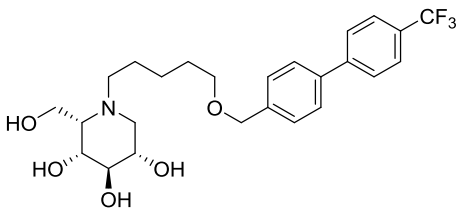
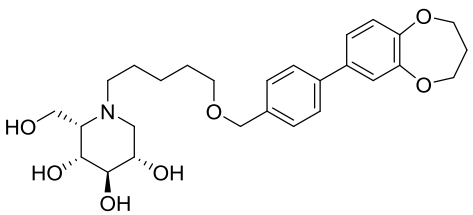
Iminosugars with dual GCS/GBA2 inhibitory activity are promising leads for drug development for the treatment of several lysosomal storage disorders. In **Chapter 5**, 16 *N*-alkyl D-glucose configured and L-idose configured DNJ derivatives were designed, synthesized and evaluated on their efficacy as dual GCS/GBA2 inhibitors. Regrettably, no outstanding new inhibitor was identified. Amongst the compounds evaluated, the one carrying a *para*-trifluorometyl substituted *N*-biphenyl moiety (L-*ido*-DNJ **34**) proved to be the most GCS/GBA2 selective compound of the series (selectivity as set against GBA1 inhibitory activity), whereas derivatives with a low logP value (such as **35**) deserve future attention as well because of their suspected improved (compared to **34**) *in vivo* activity.

***Figure 5**: Most promising GCS/GBA2 inhibitors from Chapter 5*



34



35

As also highlighted in **Chapter 5**, future research might focus on modification of the inner benzene moiety of the biphenyl substituent in the L-idose configured and D-glucose configured DNJ derivatives (for instance, **36** – **39**, Figure 6), or even modification of both benzenes (for instance, **40** – **47**).

Chapter 6 discusses the design and synthesis of a focused library comprising four configurational isomeric bis-hydroxymethyl iminosugars (**48** – **51**, Figure 7). These core structures were decorated with different aliphatic chains and the complete library was assessed on their inhibitory potential against GCS, GBA1 and GBA2. The additional (compared to the parent iminosugars) hydroxymethyl group does not bring extra potency and neither selectivity against the target enzymes.

Lack of potency towards the target enzymes may be due to steric factors, and one way to overcome this, but that would keep the symmetrical carbon at C-5 intactly, would be to condense the two hydroxyls to form an oxetane (as in **52** – **55**, Figure 8). Oxetane groups are common functional groups in medicinal chemistry and confer to drugs/drug candidates desirable features including solubility and metabolic stability.

***Figure 6**: Relevant D-gluco and L-idose configured DNJ derivatives carrying a modified biphenyl functional group*

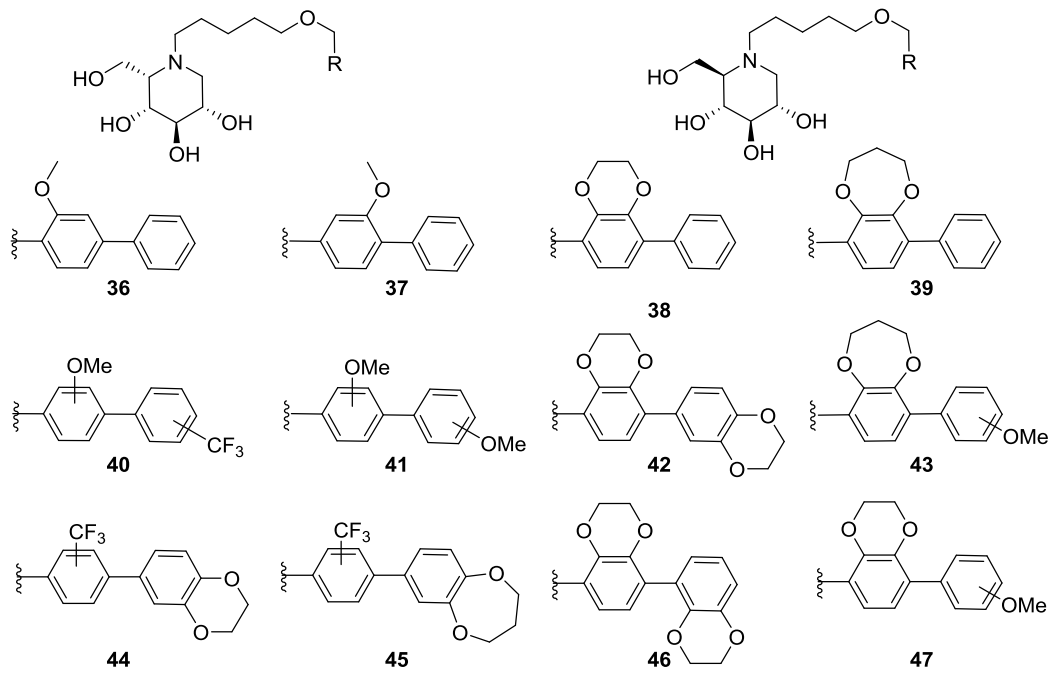


***Figure 7**: 5-Bis-hydroxymethyl DNJ compounds (**48 - 51**) described in Chapter 6*

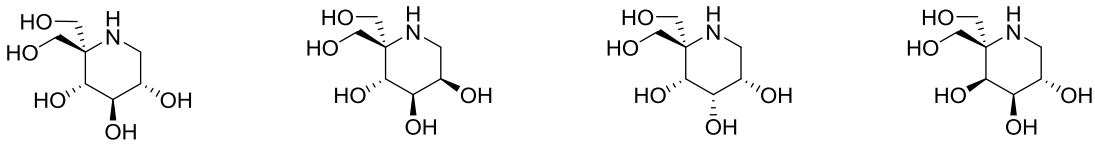
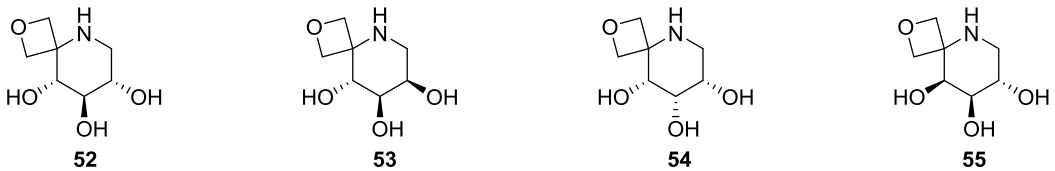
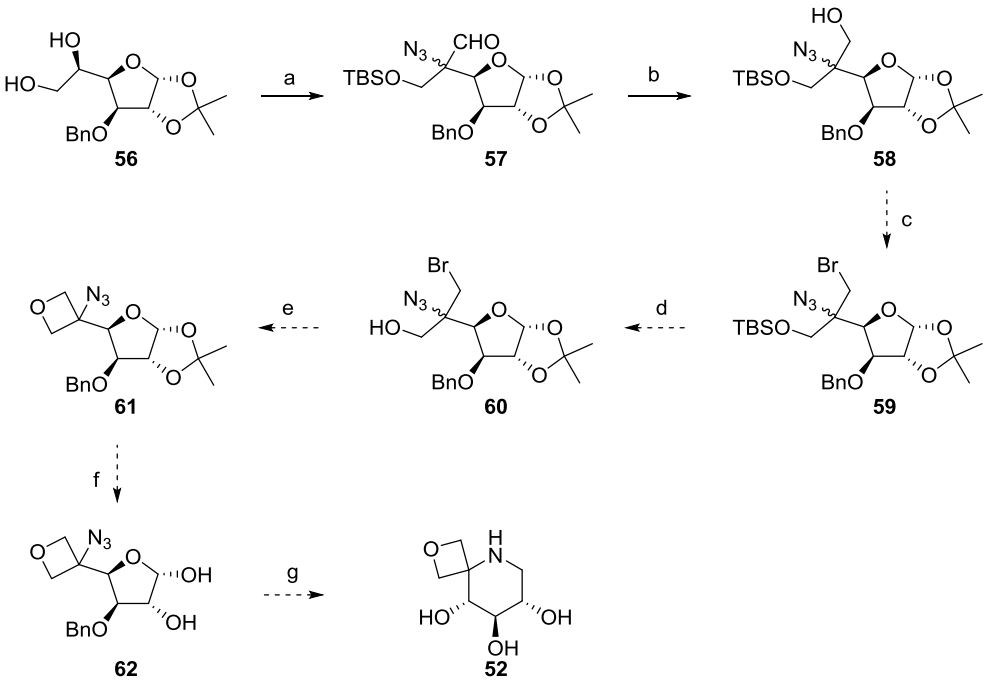


***Figure 8**: Structures of designed C-5 oxetane iminosugars*



***Scheme 2**: Designed synthesis route for 1,5-dideoxy-1,5-imino-5-oxetane-D-xylitol*

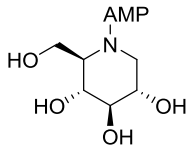


Reagents and conditions: [**a**] 1) TBSCl, TEA, DMAP, DCM; 2) PCC, DCM; 3) LDA, DCM, THF; 4) NaN_3, DMF, 115 °C; [**b**] $NaBH_4$; [**c**] CBr_4, PPh_3, DCM; [**d**] TBAF, THF; [**e**] NaOH, H_2O, MeOH; [**f**] TFA, H_2O; [**g**] H_2, Pd/C.

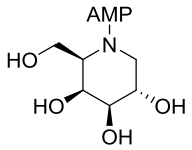
A potential route of synthesis towards compound **52** is presented in Scheme 2. The synthesis is based on diacetone-D-glucose (D-DAG), and standard protecting group manipulations have yielded compound **56**. The additional carbon and nitrogen could be introduced following a strategy similar to that described in **Chapter 6** (from D-DAG to **57**). The newly introduced hydroxylmethyl group (**58**) may be transformed to a bromide via an Appel reaction, and the bromide substituted by the liberated (**59** to **60**) OH-6 to form oxetane (**61**). The anomeric center in **61** is then to be exposed (to give **62**) using the TFA/water system after which reduction of the azide to the amine, reductive amination onto the anomeric aldehyde and concomitant debenzylation should yield **52**.

In previous studies, the inhibitory activity against GCS, GBA1 and GBA2 of a series of 1,2-dideoxynojirimycin derivatives was tested (for example, compounds **67** – **70**, Figure 9). As is evident from the depicted (Figure 9) IC_{50} values, the lack of a C-2 hydroxyl results in a loss of GCS inhibitory activity (compare the GCS inhibitory activity of **63** and **67**; **64** and **68**; **65** and **69**; **66** and **70**, Figure 9), which implies that the existence of a C-2 OH is essential.[1]

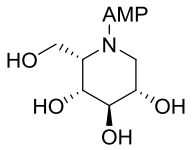
***Figure 9**: IC_{50} values of N-AMP iminosugars*



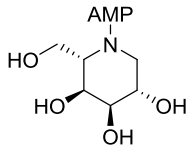
63 IC_{50} GCS 0.2 μM
IC_{50} GBA1 0.5 μM
IC_{50} GBA2 0.8 nM



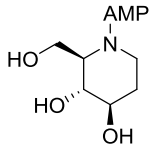
64 IC_{50} GCS 0.14 μM
IC_{50} GBA1 1 μM
IC_{50} GBA2 1 nM



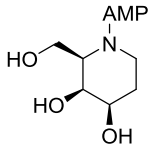
65 IC_{50} GCS 0.1 μM
IC_{50} GBA1 34 μM
IC_{50} GBA2 1 nM



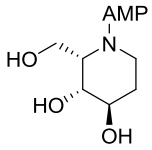
66 IC_{50} GCS 0.2 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 0.1 μM



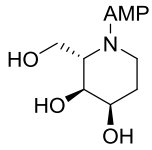
***67** IC_{50} GCS >10 μM
IC_{50} GBA1 10 μM
IC_{50} GBA2 1.0 μM



***68** IC_{50} GCS >10 μM
IC_{50} GBA1 110 μM
IC_{50} GBA2 6.5 μM



***69** IC_{50} GCS >10 μM
IC_{50} GBA1 500 μM
IC_{50} GBA2 0.5 μM

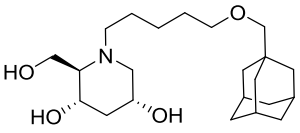


***70** IC_{50} GCS >10 μM
IC_{50} GBA1 200 μM
IC_{50} GBA2 100 μM

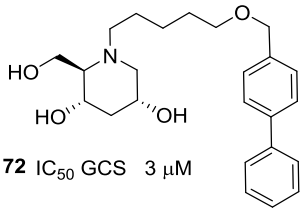
*IC_{50} values are from the literature[1]

In order to investigate the importance of C-3 OH, 1,3-dideoxynojirimycin derivatives have been synthesized and evaluated on their potency to inhibit GCS (e.g. **71** and **72**, Figure 10). It appears that removal of C-3 OH in DNJ (with the remaining chiral centers as in the parent iminosugar, deoxynojirimycin) largely abolishes GCS inhibitory activity (compare GCS inhibitory activity of **71** and **63**, **72** and **89**). It would be useful to have the full set of configurational isomers of **71** (three stereocenters – 6 stereoisomers in total besides **71** and **72**) in hand to establish their inhibitory potency against GCS but also GBA1 and GBA2, and synthetic methodology needs to be developed for this purpose.

***Figure 10**: IC_{50} values of some 1,3-dideoxynojirmmycin derivatives as GCS inhibitors*

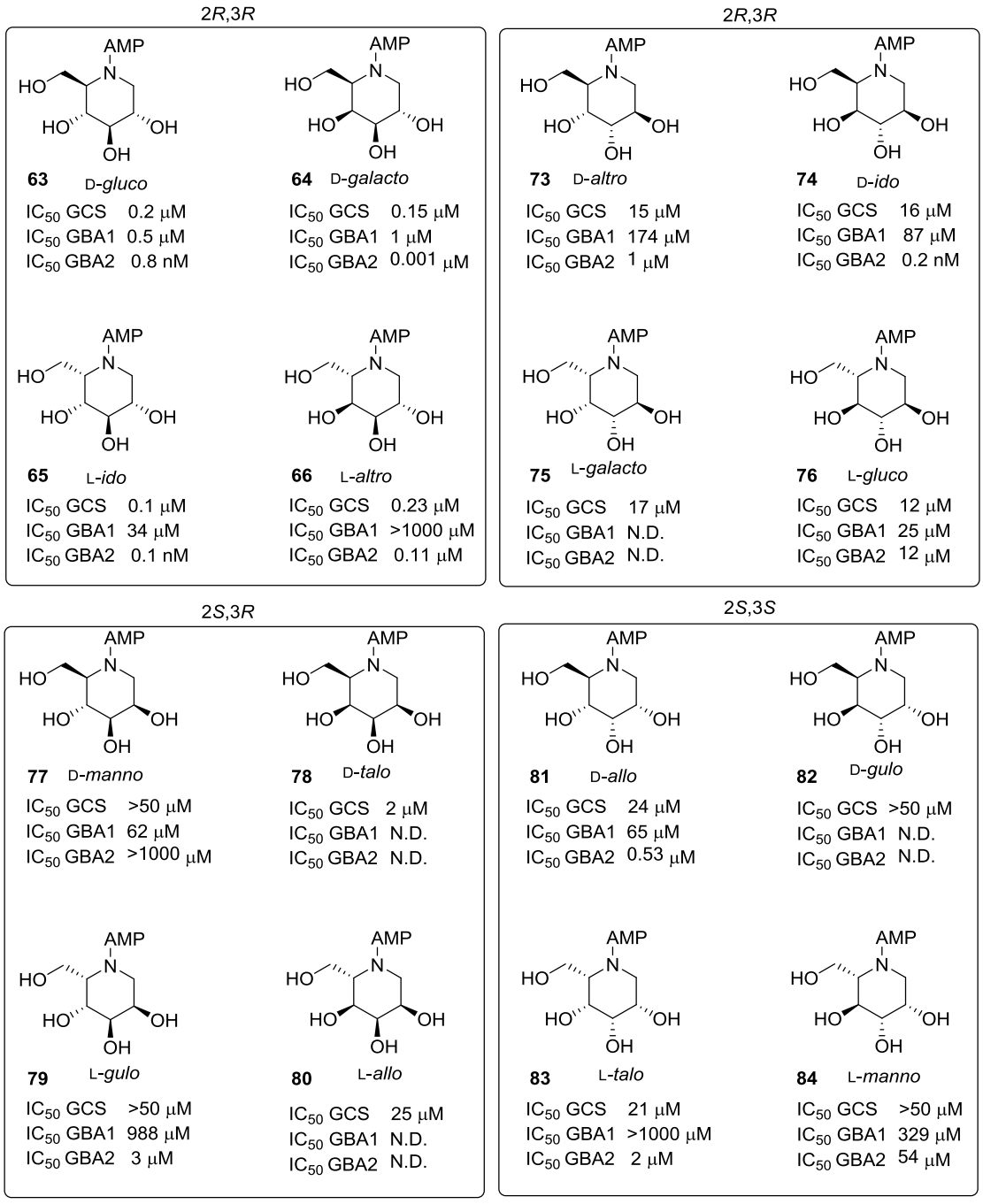


71 IC_{50} GCS ~50 μM



72 IC_{50} GCS 3 μM

***Figure 11**: IC_{50} values of AMP-alkylated DNJ congeners*

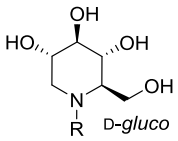


Looking closer at the IC_{50} values obtained for GCS inhibition as described in **Chapter 6**, it becomes apparent that D-glucose configured iminosugars (for instance, **63**, Figure 11) and L-idose configured iminosugars (for instance, **65**) and their C-4 epimers (for instance, D-galactose configured **64** and L-altrose configured **66**) are all able to act as GCS inhibitors. It can thus be concluded that all compounds tested and that display significant GCS inhibitory activity share one common characteristic: the (2*S*, 3*R)* configuration of the diol system (with both hydroxyls present): all relevant GCS inhibitors are found in either the D-glucose, L-idose, D-galactose or L-altrose iminosugar series.

In order to unambiguously confirm this structure-activity-relationship, the efficacy of all 16 DNJ congeners bearing the same *N*-alkyl substituent should be evaluated side-by-side on GCS, GBA1 and GBA2. Initial results towards this goal are presented in Figure 11 and concern some first inhibitory data on the complete set of 16 configurational isomers of *N*-adamantanemethoxypentyl-deoxynojirimycin. It can be seen that D-*gluco* AMP (**63**), L-*ido* AMP (**65**), D-*galacto* AMP (**64**) and L-*altro* AMP (**66**), which all have the (2*S*, 3*R*) configuration, but none of the other configurational isomers, exhibit potent GCS inhibitory activity (0.1 μM - 0.2 μM). The synthesis details of compounds **73**, **74**, **76**, **77**, **79** and **84** can be found in the experimental part.

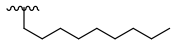
Looking at the inhibition potency of GBA1 and GBA2 as exerted by the 12 configurational isosters introduced in Figure 11, and comparing with the four lead isosteres, D-*ido* derivative **74** stands out as a promising GBA2 selective inhibitor. In order to fully capitalize on the potential of configurational and functional DNJ isosters as selective inhibitors for GCS, GBA or GBA2 as well as for unrelated glycoprocessing enzymes, it would be advantageous to have access to a focused and comprehensive library. Such a library should ideally contain all 16 configurational isomers as well as encompass all alkyl and aryl substituents found on individual DNJ isomers in the literature and that are found to have a beneficial effect, whether on enzyme inhibition potency/selectivity or on pharmacological behavior. Initial synthesis efforts have been conducted towards this goal and the resulting configurational and functional DNJ derivatives – alongside with initial GCS/GBA1/GBA2 inhibitory properties such as have been established yet – are presented in Figures 12 – 15 (see for synthesis details the experimental section).

***Figure 12**: IC_{50} values of DNJ derivatives with 2S, 3R configuration*

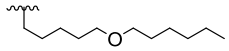


85 R = H
IC_{50} GCS >50 μM
IC_{50} GBA1 754 μM
IC_{50} GBA2 20 μM

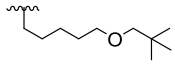
86
IC_{50} GCS 50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 0.3 μM



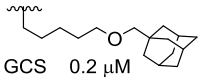
87
IC_{50} GCS 1.5 μM
IC_{50} GBA1 3 μM
IC_{50} GBA2 2 nM



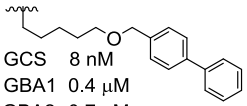
88
IC_{50} GCS 0.08μM
IC_{50} GBA1 5 μM
IC_{50} GBA2 2 nM



30
IC_{50} GCS 5 μM
IC_{50} GBA1 6 μM
IC_{50} GBA2 5 nM

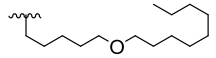


63
IC_{50} GCS 0.2 μM
IC_{50} GBA1 0.5 μM
IC_{50} GBA2 0.8 nM

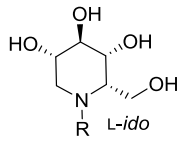


89
IC_{50} GCS 8 nM
IC_{50} GBA1 0.4 μM
IC_{50} GBA2 0.7 nM

90
IC_{50} GCS >50 μM
IC_{50} GBA1 37 μM
IC_{50} GBA2 47 nM

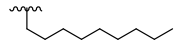


91
IC_{50} GCS 0.07 μM
IC_{50} GBA1 0.4 μM
IC_{50} GBA2 1.5 nM

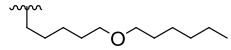


92 R = H
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 138 μM

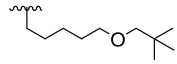
93
IC_{50} GCS 1 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 0.2 μM



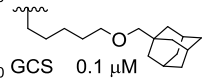
94
IC_{50} GCS 0.1 μM
IC_{50} GBA1 40 μM
IC_{50} GBA2 1 nM



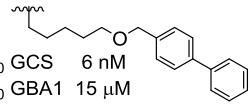
95
IC_{50} GCS 0.03 μM
IC_{50} GBA1 102 μM
IC_{50} GBA2 3 nM



31
IC_{50} GCS 1.6 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 10 nM

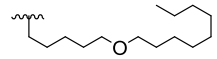


65
IC_{50} GCS 0.1 μM
IC_{50} GBA1 34 μM
IC_{50} GBA2 1 nM

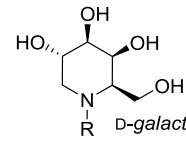


96
IC_{50} GCS 6 nM
IC_{50} GBA1 15 μM
IC_{50} GBA2 1 nM

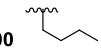
97
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 20 μM



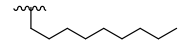
98
IC_{50} GCS 0.015 μM
IC_{50} GBA1 9 μM
IC_{50} GBA2 0.15 nM



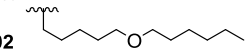
99 R = H
IC_{50} GCS >50 μM
IC_{50} GBA1 237 μM
IC_{50} GBA2 11 μM



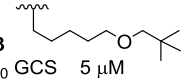
100
IC_{50} GCS 5 μM
IC_{50} GBA1 412 μM
IC_{50} GBA2 30 μM



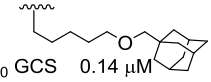
101
IC_{50} GCS 2 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 7.5 nM



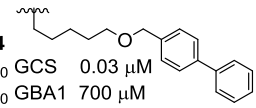
102
IC_{50} GCS 0.3μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 40 nM



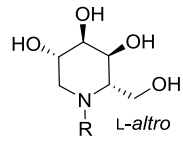
103
IC_{50} GCS 5 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 12 nM



64
IC_{50} GCS 0.14 μM
IC_{50} GBA1 1 μM
IC_{50} GBA2 1 nM

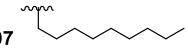


104
IC_{50} GCS 0.03 μM
IC_{50} GBA1 700 μM
IC_{50} GBA2 1 nM

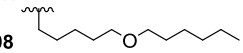


105 R = H
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 --- μM

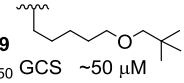
106
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 1.5 μM



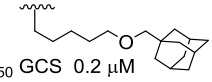
107
IC_{50} GCS 25 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 0.3 μM



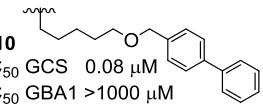
108
IC_{50} GCS 0.5 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 0.4 μM



109
IC_{50} GCS ~50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 0.7 μM

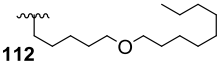


66
IC_{50} GCS 0.2 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 0.1 μM



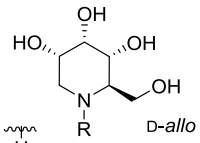
110
IC_{50} GCS 0.08 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 15 nM

111
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 108 μM



112
IC_{50} GCS 0.1μM
IC_{50} GBA1 >100 μM
IC_{50} GBA2 9 nM

***Figure 13**: IC_{50} values of DNJ derivatives with 2S, 3S configuration*



D-*allo*

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

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

115
IC_{50} GCS >50 μM
IC_{50} GBA1 306 μM
IC_{50} GBA2 0.3 μM

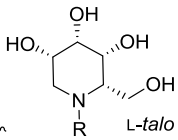
116
IC_{50} GCS >50 μM
IC_{50} GBA1 48 μM
IC_{50} GBA2 >1000 μM

117
IC_{50} GCS >50 μM
IC_{50} GBA1 815 μM
IC_{50} GBA2 17 μM

81
IC_{50} GCS 24 μM
IC_{50} GBA1 65 μM
IC_{50} GBA2 0.5 μM

118
IC_{50} GCS 2.4 μM
IC_{50} GBA1 49 μM
IC_{50} GBA2 0.4 μM

119
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 >1000 μM



L-*talo*

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

121
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 18 μM

122
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 18 μM

123
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 407 μM

124
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 333 μM

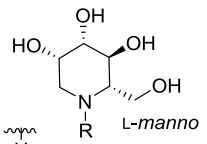
83
IC_{50} GCS 21 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 2 μM

125
IC_{50} GCS 8.5 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 30 μM

126
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 111 μM

127
IC_{50} GCS 19 μM
IC_{50} GBA1 282 μM
IC_{50} GBA2 0.4 μM

128
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 >100 μM



L-*manno*

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

130
IC_{50} GCS 2 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 7.5 nM

131
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 4 μM

132
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 361 μM

133
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 21.5 μM

84
IC_{50} GCS >50 μM
IC_{50} GBA1 329 μM
IC_{50} GBA2 55 μM

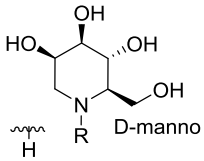
134
IC_{50} GCS 40 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 53 μM

135
IC_{50} GCS 50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 >1000 μM

136
IC_{50} GCS >50 μM
IC_{50} GBA1 310 μM
IC_{50} GBA2 16 μM

137
IC_{50} GCS >50 μM
IC_{50} GBA1 29 μM
IC_{50} GBA2 20 μM

***Figure 14**: IC_{50} values of DNJ derivatives with 2R, 3R configuration*

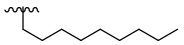


138 H

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

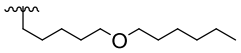
139

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



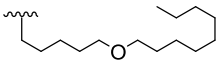
140

IC_{50} GCS >50 μM
IC_{50} GBA1 241 μM
IC_{50} GBA2 >1000 μM



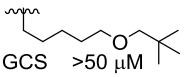
141

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



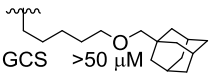
142

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



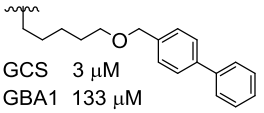
143

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



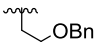
77

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



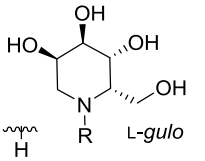
144

IC_{50} GCS 3 μM
IC_{50} GBA1 133 μM
IC_{50} GBA2 --- μM



145

IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 151 μM

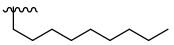


146 H

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

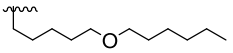
147

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



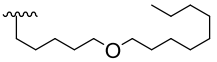
148

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



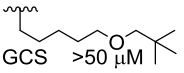
149

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



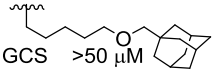
150

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



151

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



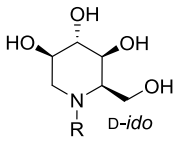
79

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

152

IC_{50} GCS 50 μM
IC_{50} GBA1 19 μM
IC_{50} GBA2 32 μM

***Figure 15**: IC_{50} values of DNJ derivatives with 2R, 3S configuration*



153 H
IC_{50} GCS >50 μM
IC_{50} GBA1 >100 μM
IC_{50} GBA2 >1000 μM

154
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 4 μM

155
IC_{50} GCS 4 μM
IC_{50} GBA1 100 μM
IC_{50} GBA2 10 nM

74
IC_{50} GCS 16 μM
IC_{50} GBA1 88 μM
IC_{50} GBA2 0.2 nM

156
IC_{50} GCS 11 μM
IC_{50} GBA1 2.3 μM
IC_{50} GBA2 2 nM

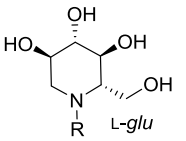
157 OBn
IC_{50} GCS >50 μM
IC_{50} GBA1 98 μM
IC_{50} GBA2 143 μM

158 OH
IC_{50} GCS >50 μM
IC_{50} GBA1 ~100 μM
IC_{50} GBA2 >1000 μM

159
IC_{50} GCS 10 μM
IC_{50} GBA1 25 μM
IC_{50} GBA2 0.7 μM

160
IC_{50} GCS 50 μM
IC_{50} GBA1 32 μM
IC_{50} GBA2 11 μM

32
IC_{50} GCS 7 μM
IC_{50} GBA1 387 μM
IC_{50} GBA2 4 nM



161 H
IC_{50} GCS >50 μM
IC_{50} GBA1 730μM
IC_{50} GBA2 >1000 μM

162
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 >100 μM

163
IC_{50} GCS >50 μM
IC_{50} GBA1 40 μM
IC_{50} GBA2 50 μM

76
IC_{50} GCS 12 μM
IC_{50} GBA1 25.5 μM
IC_{50} GBA2 12 μM

164
IC_{50} GCS 1.4 μM
IC_{50} GBA1 57 μM
IC_{50} GBA2 3 μM

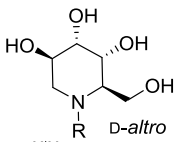
165 OBn
IC_{50} GCS 50 μM
IC_{50} GBA1 ~1000 μM
IC_{50} GBA2 0.3 μM

166 OH
IC_{50} GCS 50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 22 μM

167
IC_{50} GCS 9 μM
IC_{50} GBA1 24 μM
IC_{50} GBA2 4 μM

168
IC_{50} GCS 20 μM
IC_{50} GBA1 429 μM
IC_{50} GBA2 49 μM

169
IC_{50} GCS >50 μM
IC_{50} GBA1 198 μM
IC_{50} GBA2 208 μM



170 H
IC_{50} GCS N.D.
IC_{50} GBA1 N.D.
IC_{50} GBA2 N.D.

171
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 552 μM

172
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 8 μM

73
IC_{50} GCS 15 μM
IC_{50} GBA1 174 μM
IC_{50} GBA2 1 μM

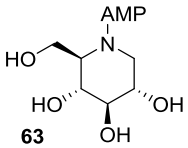
173
IC_{50} GCS >50 μM
IC_{50} GBA1 71 μM
IC_{50} GBA2 6 μM

174 OBn
IC_{50} GCS >50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 126 μM

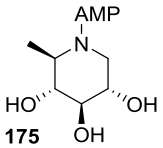
One literature study, describes the synthesis and evaluation of 1,6-dideoxynojirimycin (**175**) and xylose-DNJ (**176**).[1] Compared to DNJ derivative **63** (Figure 16) both compounds

proved to be less potent as GCS inhibitors, with the xylose-configured one less active than the quinuvose-configured one. This result suggests that the functional group at C-6 contributes to GCS inhibitory activity.

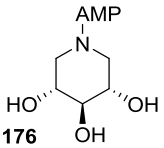
***Figure 16**: IC_{50} values of DNJ-AMP, 6-deoxy-DNJ AMP and 6-dehydroxy-DNJ-AMP*



63
IC_{50} GCS 0.2 μM
IC_{50} GBA1 0.5 μM
IC_{50} GBA2 0.8 nM



175
*IC_{50} GCS 0.8 μM
*IC_{50} GBA1 0.3 μM
*IC_{50} GBA2 30 nM

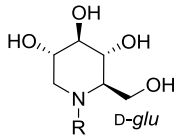


176
*IC_{50} GCS >10 μM
*IC_{50} GBA1 2 μM
*IC_{50} GBA2 800 nM

*IC_{50} data from the literature[1]

Based on the data above, substitution of the C6-OH in **63** with an electron-withdrawing functional group may yield a conceptually new, potent and potentially selective GCS inhibitor. Fluorine is a widely used hydroxyl isostere[2] that has about the same size and is comparatively more electron-withdrawing, and substituting C6-OH in **63** with fluorine therefore appeared an attractive strategy.

***Figure 17**: IC_{50} values of DNJ and 6-deoxy-6-fluoro-DNJ derivatives*



86
IC_{50} GCS 50 μM
IC_{50} GBA1 >1000 μM
IC_{50} GBA2 0.3 μM

87
IC_{50} GCS 1.5 μM
IC_{50} GBA1 3 μM
IC_{50} GBA2 2 nM

88
IC_{50} GCS 0.08μM
IC_{50} GBA1 5 μM
IC_{50} GBA2 2 nM

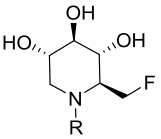
30
IC_{50} GCS 5 μM
IC_{50} GBA1 6 μM
IC_{50} GBA2 5 nM

63
IC_{50} GCS 0.2 μM
IC_{50} GBA1 0.5 μM
IC_{50} GBA2 0.8 nM

89
IC_{50} GCS 8 nM
IC_{50} GBA1 0.4 μM
IC_{50} GBA2 0.7 nM

90
IC_{50} GCS >50 μM
IC_{50} GBA1 37 μM
IC_{50} GBA2 47 nM

91
IC_{50} GCS 0.07 μM
IC_{50} GBA1 0.4 μM
IC_{50} GBA2 1.5 nM



177
IC_{50} GCS 34 μM
IC_{50} GBA1 298 μM
IC_{50} GBA2 2 μM

178
IC_{50} GCS 13 μM
IC_{50} GBA1 2 μM
IC_{50} GBA2 16 nM

179
IC_{50} GCS 1 μM
IC_{50} GBA1 2.5 μM
IC_{50} GBA2 31 nM

180
IC_{50} GCS 9 μM
IC_{50} GBA1 10 μM
IC_{50} GBA2 68 nM

181
IC_{50} GCS 1.5 μM
IC_{50} GBA1 1 μM
IC_{50} GBA2 4 nM

182
IC_{50} GCS 0.4 μM
IC_{50} GBA1 1 μM
IC_{50} GBA2 5 nM

183
IC_{50} GCS 34 μM
IC_{50} GBA1 298 μM
IC_{50} GBA2 2 μM

184
IC_{50} GCS 0.7 μM
IC_{50} GBA1 0.8 μM
IC_{50} GBA2 7 nM

However, 6-deoxy-6-fluoro-AMP-DNJ (**181**, Figure 17) turned out to be a comparatively poor GCS inhibitor. The same trend is reflected in some *N*-alkyl derivatives when looking at a

side-by-side comparison (compare compounds **177** – **183** with their 6-hydroxy counterparts) and GBA1/GBA2 inhibition potency appears affected by the OH-to-F substitution as well. A tentative conclusion may be that the hydrogen-bond-donating properties of the C6-OH (and not so much the hydrogen-bond accepting properties – though arguably a fluorine partakes in neither) are what makes DNJ derivatives bearing this substituent more potent against the three enzymes tested. Nevertheless, the developed methodology to introduce a fluorine at C-6 allows for synthesis of C6-fluorine-modified, configurational DNJ isomers as well, and it may well be that the O6-for-F substitution is beneficial for DNJ derivatives targeting glycoprocessing enzymes other than the ones subject of this Thesis.

Experimental Section

Enzyme inhibition assays: The inhibitory potencies (IC_{50} values) of the final compounds for GCS, GBA1 and GBA2 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.[3] 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.[4] 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 0.2% (w/v) sodium taurocholate. 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 the 4-methylumbeliferyl-β-D-glucoside as substrate.[4] 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 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.[5] 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 provided by GE-Healthcare polymere HW-40S from Toyopearl, 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 A: Alkylation of iminosugars. To a mixture of the 1-bromo-5-alkyloxy-pentane (1.5 eq) and di-isopropylethylamine (DiPEA, 3 eq) was added a solution of iminosugar (1 eq) in DMF (0.2M). The reaction mixture was stirred overnight at 70 °C. After cooling to room temperature, the mixture was filtered and concentrated. The crude compound was purified using silica gel column chromatography (0% → 20% methanol in DCM + 1% NH_4OH).

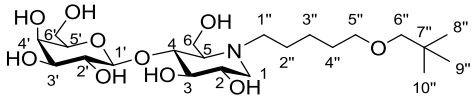
General Procedure B: Alkylation of iminosugars. To a mixture of the bromide chain (1.5 eq) and K_2CO_3 (3eq) was added a solution of the (glycosylated) iminosugar (1eq) in DMF (0.2 M). The reaction suspension was stirred at 85 °C for 18 hours. After cooling to room temperature, the mixture was filtered and concentrated. The crude compound was purified with HPLC.

General Procedure C: Alkylation of protected glycosylated iminosugars. Glycosylated disaccharide iminosugar (0.2 mmol), aldehyde chain (0.3 mmol), AcOH (1.6 mmol), $NaCNBH_3$ (0.8 mmol), Na_2SO_4 (desiccant) and MeOH (2 mL) was mixed at 0 °C and stirred overnight, allowing the temperature to reach r.t. After TLC analysis showed the completely consumption of starting material (4:1, PE:EtOAc), the mixture was filtered and concentrated. The residue was dissolved in DCM (15 mL) and washed with aq. $NaHCO_3$ (10%), dried (Na_2SO_4), filtered and concentrated. The residue was purified using silica gel column chromatography (19:1 → 9:1→ 17:3 → 4:1, PE:EtOAc).

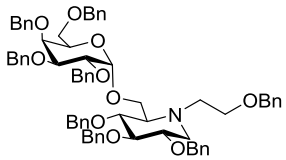
General Procedure D: Catalytic Hydrogenation of protected glycosylated *N*-alkyl DNJ. Protected glycosylated DNJ derivative (1eq) was dissolved in MeOH/DMF (1 mM, 2:1; v:v), and the solution was flushed with argon (3 x). After which a catalytic amount of Pd/C (20%) was added. The mixture was kept shaking under H_2 atmosphere (4 bar) overnight. After TLC analysis showed the absent of benzyl groups, the crude product was purified on size-exclusion column.

Synthesis of alkylated glycosylated-1-deoxynojirimycin

***Figure 18**: Proton and carbon NMR numbering of N-alkylated glycosylated iminosugars:*

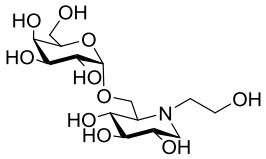


2,3,4-Tri-O-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-*N*-ethan-2-(benzyloxy)-1-deoxynojirimycin (9):



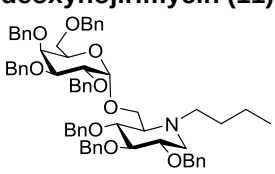
A mixture of DCM/MeOH (1:1, v:v, 15 mL) and *melibio*-DNJ (0.19 g, 0.20 mmol) was cooled in an ice bath. AcOH (92 µL, 1.6 mmol, 8 eq in 1 mL MeOH), 2-(benzyloxy)acetaldehyde (48.1 mg, 0.32 mmol, 1.6 eq in 1 mL DCM) and $NaCNBH_3$ (50.3 mg, 0.8 mmol, 4 eq) were added in respective order. The mixture was stirred overnight allowing warming up to r.t. After evaporating the volatiles, DCM (20 mL) was added to the residue and the organic layer was washed with sat. aq. $NaHCO_3$ (15 mL), dried (Na_2SO_4) filtered and concentrated. The residue was purified on silica gel column (9:1 → 4:1, PE:EtOAc) to gain **9** in 64% yield (140 mg, 0.128 mmol). R_F = 0.54 (7:3, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.11 (m, 40H, H_{Ar} Bn), 4.99 (d, *J* = 3.9 Hz, 1H, H-1'), 4.96 – 4.23 (m, 16H, 8 x CH_2 Bn), 4.02 (dd, *J* = 9.3, 3.5 Hz, 1H, H-2'), 3.98 – 3.83 (m, 5H, H-3', H-4, H-4, H_2-6'), 3.61 – 3.47 (m, 6H, H-2, H_2-2", H-3, H-5', H-6a), 3.43 (dd, *J* = 9.0, 5.7 Hz, 1H, H-6b), 3.20 (dd, *J* = 11.5, 4.5 Hz, 1H, H-1a), 3.03 (dt, *J* = 11.0, 5.5 Hz, 1H, H-1"a), 2.89 (dt, *J* = 14.2, 5.2 Hz, 1H, H-1"b), 2.53 (d, *J* = 7.4 Hz, 1H, H-5), 2.32 (t, *J* = 10.8 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.1 – 138.1 (C_q Bn), 128.6 – 127.5 (CH_{Ar} Bn), 98.3 (C-1'), 87.3 (C-3), 78.6 (C-2), 78.5 (C-4), 76.7 (C-2'), 75.4, 75.2 (2 x CH_2 Bn), 75.0 (C-3'), 74.9, 73.5, 73.1, 73.1, 72.9, 72.8 (6 x CH_2 Bn), 69.9 (C-4'), 68.8 (C-6), 67.6 (C-2"), 65.7 (C-6'), 64.9 (C-5), 55.2 (C-1), 52.0 (C-1"). $[\alpha]^{20}_D$ = +31.8 (c = 1.0, $CHCl_3$). IR/cm^{-1}: 3029, 2911, 2852, 1496, 1453, 1321, 1207, 1093, 1061, 1027.

6-*O*-(α-D-Galactopyranosyl)-*N*-hydroxyethyl-1-deoxynojirimycin (10):



9 (0.13 g, 0.12 mmol) was subjected to the general procurer D to generate **10** (40.1 mg, 0.109 mmol) in a yield of 91%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.82 (d, *J* = 3.6 Hz, 1H, H-1'), 4.30 (d, *J* = 11.0 Hz, 1H, H-6a), 4.17 (dd, *J* = 10.9, 1.8 Hz, 1H, H-6b), 3.92 (d, *J* = 2.7 Hz, 1H, H-4'), 3.85 (t, *J* = 6.1 Hz, 1H, H-5'), 3.78 (dd, *J* = 10.1, 3.0 Hz, 1H, H-2'), 3.75 (dd, *J* = 7.4, 3.6 Hz, 2H, H_2-2"), 3.73 (dd, *J* = 7.5, 4.0 Hz, 1H, H-3'), 3.70 (dd, *J* = 6.0, 3.1 Hz, 2H, H_2-6'), 3.64 (dd, *J* = 10.9, 2.2 Hz, 1H, H-6a), 3.52 (ddd, *J* = 10.6, 9.4, 4.9 Hz, 1H, H-2), 3.43 (t, *J* = 9.4 Hz, 1H, H-4), 3.18 (t, *J* = 9.1 Hz, 1H, H-3), 3.15 (dd, *J* = 11.5, 4.8 Hz, 1H, H-1b), 2.96 (dt, *J* = 13.7, 6.2 Hz, 1H, H-1b"), 2.78 (dt, *J* = 13.9, 5.7 Hz, 1H, H-1a"), 2.46 (dd, *J* = 9.7, 2.4 Hz, 1H, H-5), 2.43 (dd, *J* = 11.4, 10.7 Hz, 1H, H-1a). ^{13}C NMR (100 MHz, $CDCl_3$) δ 100.3 (C-1'), 80.4 (C-3), 72.4 (C-5'), 71.7 (C-2'), 71.4 (C-4), 70.9 (C-4'), 70.7 (C-3'), 70.6 (C-2), 66.1 (C-5), 63.6 (C-6), 62.5 (C-6'), 58.8 (C-2"), 58.3 (C-1), 55.0 (C-1"). $[\alpha]^{20}_D$ = +68.4 (c = 0.5, MeOH). IR/cm^{-1}: 3256, 2894, 1558, 1409, 1343, 1151, 1081, 1038. HRMS: found 370.17082 $[C_{14}H_{28}NO_{10}+H]^+$, calculated for $[C_{14}H_{28}NO_{10}+H]^+$ 370.17077.

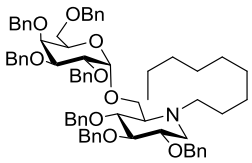
2,3,4-Tri-O-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-*N*-butyl-1-deoxynojirimycin (11).



Protected *melibio*-DNJ (0.19 g, 0.2 mmol) was subjected to the general procedure C to generate **11** (0.18 g, 0.18 mmol) in a yield of 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.14 (m, 35H, H_{Ar} Bn), 5.03 (d, *J* = 3.2 Hz, 1H H-1'), 4.99 – 4.27 (m, 14H, 7 x CH_2 Bn), 4.04 (dd, *J* =

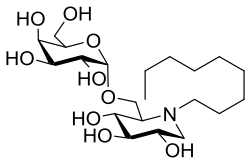
10.2, 2.8 Hz, 1H, H-2'), 4.00 – 3.92 (m, 3H, H-3', H-4', H-5'), 3.89 (dd, *J* = 11.8, 3.4 Hz, 1H, H-6a), 3.83 (dd, *J* = 11.7, 1.5 Hz, 1H, H-6b), 3.62 – 3.42 (m, 5H, H-2, H-3, H-4, H_2-6'), 3.08 (dd, *J* = 11.3, 4.6 Hz, 1H, H-1a), 2.78 (m, 1H, H-1"a), 2.55 (m, 1H, H-1"a), 2.39 (d, *J* = 9.3 Hz, 1H, H-5), 2.15 (t, *J* = 10.7, 1H, H-1"b), 1.32 – 1.42 (m, 2H, H_2-2"), 1.15 – 1.25 (m, 2H, H_2-3"), 0.85 (t, *J* = 7.3 Hz, 3H, H_3-4"). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.2 – 138.1 (7 x C_q Bn), 128.5 – 127.5 (CH_{Ar} Bn), 98.2 (C-1'), 87.4 (C-3), 78.8 (C-4), 78.8 (C-2), 78.7 (C-3'), 76.8 (C-2'), 75.3 (CH_2 Bn), 75.2 (C-4'), 74,9, 73.5, 73.0, 72.8, (CH_2 Bn), 69.9 (C-5'), 68.9 (C-6'), 65.0 (C-5), 65.0 (C-6), 54.4 (C-1), 52.8 (C-1"), 26.6 (C-2"), 20.8 (C-3"), 14.2 (C-4"). $[\alpha]^{20}_D$ = +11.8 (c = 1.0, $CHCl_3$). IR/cm^{-1}: 3030, 2924, 2870, 1497, 1454, 1362, 1207, 1092, 1059, 1028. HRMS: found 1012.53571 $[C_{21}H_{41}NO_9+H]^+$, calculated for $[C_{21}H_{41}NO_9+H]^+$ 1012.53581.

2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-*N*-nonyl-1-deoxynojirimycin (12):



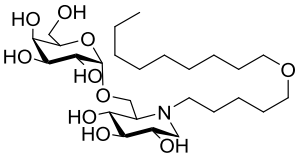
Protected *melibio*-DNJ (0.19 g, 0.2 mmol) was subjected to the general procedure C to generate **12** (0.20 g, 0.19 mmol) in a yield of 93%. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.08 (m, 35H, H_{Ar} Bn), 5.75 (d, *J* = 3.3 Hz, 1H, H-1'), 5.03 – 4.23 (m, 14H, 7 x CH_2 Bn), 4.11 (t, *J* = 8.2 Hz, 1H, H-4'), 3.99 (t, *J* = 9.2 Hz, 1H, H-4), 3.83 – 3.57 (m, 6H, H-2', H-3, H-3', H-5', H-6a, H-6'a), 3.56 – 3.48 (m, 3H, H-2, H-6b, H-6'b), 3.08 (dd, *J* = 11.1, 4.7 Hz, 1H, H-1'a), 2.58 – 2.48 (m, 3H, H_2-1", H-5), 2.33 (t, *J* = 10.7 Hz, 1H, H-1'b), 1.47 – 1.15 (m, 12H, H_2-2" – H_2-7"), 1.12 – 1.02 (m, 2H, H_2-8"), 0.89 (t, *J* = 6.9 Hz, 3H, H_3-9"). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 139.1 – 137.8 (C_q Bn), 128.4 – 126.8 (CH_{Ar} Bn), 95.8 (C-1'), 86.3 (C-3), 82.1 (C-4), 79.7 (C-2), 78.6 (C-3'), 77.7 (C-2'), 75.6, 74.9, 73.6, 73.0, 72.9, 72.8, 72.4 (7 x CH_2 Bn), 72.1 (C-4'), 70.9 (C-5'), 68.2 (C-6'), 65.8 (C-6), 63.0 (C-5), 53.4 (C-1), 52.6 (C-1"), 32.0, 29.6, 29.6, 29.3, 27.4, 24.1, 22.8, 14.2 (C-2'' – C-9''). $[\alpha]^{20}_D$ = +30.4 (c = 2.1, $CHCl_3$). IR/cm^{-1}: 3063, 3030, 2922, 2855, 1497, 1454, 1359, 1207, 1091, 1059, 1028.

6-*O*-(α-D-Galactopyranosyl)-*N*-nonyl-1-deoxynojirimycin (13):



12 was subjected to the general procedure D to generate **13** (25.4 mg, 0.06 mmol) in a yield of 89%. ^{1}H NMR (400 MHz, MeOD) δ 4.92 (d, *J* = 3.9 Hz, 1H, H-1'), 4.33 (d, *J* = 11.7 Hz, 1H, H-6a), 3.91 (d, *J* = 3.5 Hz, 1H, H-3'), 3.89 (d, *J* = 3.8 Hz, 1H, H-2'), 3.81 (t, *J* = 5.9 Hz, 1H, H-5'), 3.74 (d, *J* = 3.3 Hz, 1H, H-4'), 3.71 (d, *J* = 6.0 Hz, 2H, H_2-6'), 3.68 (dd, *J* = 10.6, 5.8 Hz, 1H, H-6b), 3.67 (t, *J* = 11.6 Hz, 1H, H-2), 3.62 (t, *J* = 9.8 Hz, 1H, H-4), 3.54 (dd, *J* = 12.1, 4.8 Hz, 1H, H-1a), 3.37 (t, *J* = 9.2 Hz, 1H, H-3), 3.33 – 3.29 (m, 1H, H-1''a), 3.26 (d, *J* = 10.0 Hz, 1H, H-5), 3.13 (td, *J* = 12.5, 5.5 Hz, 1H, H-1''b), 3.03 (t, *J* = 11.7 Hz, 1H, H-1b), 1.77 – 1.71 (m, 2H, H_2-2''), 1.46 – 1.22 (m, 12H, H_2-3'', H_2-4', H_2-5'', H_2-6'', H_2-7'', H_2-8''), 0.91 (t, *J* = 7.0 Hz, 3H, H_3-9''). ^{13}C NMR (100 MHz, MeOD) δ 100.0 (C-1'), 78.2 (C-3), 72.8 (C-5'), 71.3 (C-4'), 70.8 (C-3'), 70.0 (C-2'), 69.0 (C-4), 68.0 (C-2), 66.2 (C-5), 62.5 (C-6'), 60.3 (C-6), 55.1 (C-1), 54.4 (C-1''), 33.0, 30.5, 30.3, 30.3, 27.7, 24.2, 23.7 (C-2''- C-8''), 14.4 (C-9''). HRMS: found 452.28500 $[C_{21}H_{41}NO_9+H]^+$, calculated for $[C_{21}H_{41}NO_9+H]^+$ 452.28541.

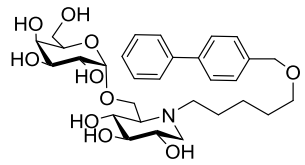
6-*O*-(α-D-Galactopyranosyl)-*N*-[5-(nonyloxy)pentyl]-1-deoxynojirimycin (14):



Melibio-DNJ (**1**, 32.0 mg, 0.1 mmol) was subjected to the general procedure B to generate **14** (16.9 mg, 0.04 mmol) in a yield of 32%. ^{1}H-NMR (400 MHz, MeOD) δ 4.91 (d, *J* = 4.6 Hz, 1H, H-1'), 4.30 (d, *J* = 11.4 Hz, 1H, H-6'a), 3.93 – 3.89 (m, 1H, H-4'), 3.91 – 3.83 (m, 1H, H-4), 3.82 (t, *J* = 6.1 Hz, 1H, H-5'), 3.76 – 3.70 (m, 3H, H_2-6, H-6'b), 3.69 – 3.57 (m, 2H, H-2, H-3'), 3.52 – 3.40 (m, 6H, H_2-1'', H_2-6", H_2-5"), 3.36 (d, *J* = 9.1 Hz, 1H, H-3), 3.28 – 3.20 (m, 1H, H-1a), 3.19 – 3.04 (m, 2H, H-1b, H-5), 1.81 – 1.71 (m, 2H, H_2-2"), 1.68 – 1.60 (m, 2H, H_2-4"), 1.60 – 1.52 (m, 2H, H_2-7"), 1.50 – 1.40 (m, 2H, H_2-3"), 1.33 (m, 12H, H_2-8'', H_2-9'', H_2-10'', H_2-11'', H_2-12'', H_2-13''), 0.90 (t, *J* = 6.8 Hz, 3H, H_3-14").

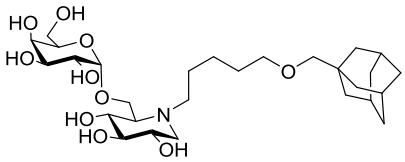
^{13}C NMR (100 MHz, MeOD) δ 100.1 (C-1'), 78.3 (C-3), 72.7 (C-5'), 72.1 (C-6''), 71.5 (C-5''), 71.3 (C-2'), 70.8 (C-4), 70.1 (C-4'), 69.3 (C-3'), 68.3 (C-2), 66.0 (C-5), 62.5 (C-6), 60.6 (C-6'), 55.3 (C-1''), 54.3 (C-1), 33.1, 30.8, 30.7, 30.6, 30.4, 30.2, 27.3, 24.6, 23.9, 23.7 (C-2'' – C-4'', C-7'' – C-13''), 14.5 (C-14''). $[\alpha]^{20}_D$ = +48.2 (c = 0.34, MeOH). IR/cm^{-1}: 3350, 2926, 2855, 1672, 1458, 1431, 1366, 1204, 1134, 1080, 1042. HRMS: found 538.35812 $[C_{26}H_{51}NO_{10}+H]^+$, calculated for $[C_{26}H_{51}NO_{10}+H]^+$ 538.35857.

6-*O*-(α-D-Galactopyranosyl)-*N*-[(biphenyl-4-yl-methoxy)-pentyl]-1-deoxynojirimycin (15):



Melibio-DNJ (**1**) was subjected to the general procedure A to generate **15** (7.5 mg, 0.01 mmol) in a yield of 13%. ^{1}H NMR (600 MHz, MeOD) δ 7.64 – 7.62 (m, 4H, H_{Ar} BiPh), 7.48 – 7.43 (m, 4H, H_{Ar} BiPh), 7.38 – 7.33 (m, 1H, H_{Ar} BiPh), 4.94 (d, *J* = 4.0 Hz, 1H, H-1'), 4.57 (s, 2H, H_2-6''), 4.33 (d, *J* = 11.7 Hz, 1H, H-6'a), 3.93 (d, *J* = 2.8 Hz, 1H, H-4), 3.91 (dd, *J* = 10.0, 3.9 Hz, 1H, H-4'), 3.83 (t, *J* = 6.1 Hz, 1H, H-5'), 3.75 (dd, *J* = 10.1, 3.4 Hz, 1H, H-2'), 3.73 (d, *J* = 6.0 Hz, 2H, H_2-6), 3.69 (dd, *J* = 11.7, 2.8 Hz, 1H, H-6'b), 3.70 – 3.66 (m, 1H, H-2), 3.64 (dd, *J* = 10.3, 9.2 Hz, 1H, H-3'), 3.59 (t, *J* = 6.2 Hz, 2H, H-5''), 3.55 (dd, *J* = 12.1, 4.9 Hz, 1H, H-1a), 3.38 (t, *J* = 9.2 Hz, 1H, H-3), 3.37 – 3.34 (m, 1H, H-1''a), 3.27 (d, *J* = 11.1 Hz, 1H, H-5), 3.17 (td, *J* = 12.5, 5.1 Hz, 1H, H-1''b), 3.05 (t, *J* = 11.8 Hz, 1H, H-1b), 1.91 – 1.76 (m, 2H, H_2-2''), 1.76 – 1.69 (m, 2H, H_2-4''), 1.58 – 1.49 (m, 2H, H_2-3''). ^{13}C NMR (150 MHz, MeOD) δ 140.6 – 126.4 (C_{Ar}), 98.6 (C-1'), 76.8 (C-3), 72.3 (C-6''), 71.3 (C-5'), 69.8 (C-2'), 69.6 (C-5''), 69.3 (C-4), 68.6 (C-4'), 67.6 (C-3'), 66.5 (C-2), 64.7 (C-5), 61.1 (C-6), 58.9 (C-6'), 53.7 (C-1), 52.9 (C-1''), 28.7 (C-4''), 23.2 (C-3''), 22.5 (C-2''). $[\alpha]^{20}_D$ = +41.4 (c = 0.5, MeOH); IR/cm^{-1}: 3550, 3062, 2302, 1716, 1699, 1558, 1521, 1506, 1489, 1394, 1338, 1203, 1139, 1080, 1064, 1039. HRMS: found 578.29407 $[C_{30}H_{43}NO_{10}+H]^+$, calculated for $[C_{30}H_{43}NO_{10}+H]^+$ 578.29597.

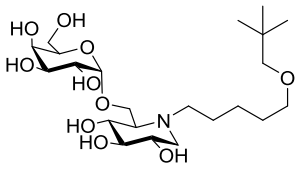
6-*O*-(α-D-Galactopyranosyl)-*N*-[5-(adamantan-1-yl-methoxy)-pentyl]-1-deoxynojirimycin (16):



Melibio-DNJ (**1**) was subjected to the general procedure A to generate **16** (5.6 mg, 0.01 mmol) in a yield of 10%**.** ^{1}H NMR (600 MHz, MeOD) δ 4.95 (d, *J* = 3.9 Hz, 1H, H-1'), 4.35 (d, *J* = 11.7 Hz, 1H, H-6'a), 3.94 (dd, *J* = 3.4, 1.0 Hz, 1H, H-4), 3.91 (dd, *J* = 10.0, 3.9 Hz, 1H, H-4'), 3.83 (t, *J* = 6.1 Hz, 1H, H-5'), 3.76 (dd, *J* = 10.1, 3.3 Hz, 1H, H-2'), 3.73 (d, *J* = 6.1 Hz, 2H, H_2-6), 3.72 – 3.67 (m, 2H, H-6'b, H-2), 3.65 (t, *J* = 9.9 Hz, 1H, H-3), 3.56 (dd, *J* = 12.1, 4.9 Hz, 1H, H-1a), 3.44 (t, *J* = 6.2 Hz, 2H, H_2-5''), 3.39 (t, *J* = 9.3 Hz, 1H, H-3), 3.36 – 3.34 (m, 1H, H-1''a), 3.28 (d, *J* = 10.5 Hz, 1H, H-5), 3.17 (td, *J* = 12.5, 5.0 Hz, 1H, H-1''b), 3.06 (t, *J* = 11.8 Hz, 1H, H-1b), 2.98 (s, 2H, H_2-6''), 1.97 (t, *J* = 3.1 Hz, 3H, 3 x CH ada), 1.89 – 1.72 (m, 2H, H-2''), 1.81 –1.68 (m, 6H, CH_2 ada), 1.68 – 1.64 (m, 2H, H_2-4''), 1.58 (d, *J* = 2.9 Hz, 6H, 3 x CH_2 ada), 1.52 – 1.47 (m, 2H, H_2-3''). ^{13}C NMR (150 MHz, MeOD) δ 100.2 (C-1'), 83.3 (C-6''), 78.3 (C-3), 72.9 (C-5'), 72.3 (C-5''), 71.4 (C-2'), 70.9 (C-4), 70.1 (C-4'), 69.1 (C-3'), 68.1 (C-2), 66.2 (C-5), 62.6 (C-6), 60.4 (C-6'), 55.2 (C-1), 54.4 (C-1''), 41.0 (CH_2 ada), 38.4 (CH_2 ada), 35.2 (C_q ada), 30.3 (C-4''), 29.8 (CH ada), 24.7 (C-3''), 24.0 (C-2''). $[\alpha]^{20}_D$ = +31.5 (c = 0.2, MeOH). IR/cm^{-1}: 3385, 3161, 2374, 2349, 2320, 2063, 1683, 1558, 1506, 1436, 1207, 1138, 1082, 1039. HRMS: found 560.34239 $[C_{28}H_{49}NO_{10}+H]^+$, calculated for $[C_{28}H_{49}NO_{10}+H]^+$ 560.34292.

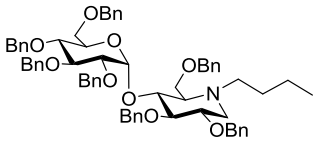
6-*O*-(α-D-Galactopyranosyl)-*N*-[5-(3,3-dimethyl-1-propyloxy)pentyl]-1-deoxynojirimycin (17):

Melibio-DNJ (**1**, 32.5 mg, 0.1 mmol) was subjected to the general procedure B to generate **17** (13.0 mg, 27.0 mmol) in a yield of 27%. ^{1}H NMR (400 MHz, MeOD) δ 4.93 (d, *J* = 3.8 Hz, 1H, H-1'), 4.33 (d, *J* = 11.6 Hz, 1H, H-6'a), 3.93 – 3.87 (m, 2H, H-4, H-4'), 3.81 (t, *J* = 6.0 Hz, 1H, H-5'),



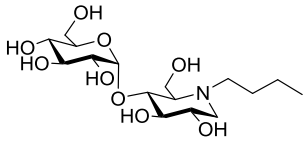
3.78 – 3.68 (m, 3H, H-2', H_2-6), 3.69 – 3.59 (m, 2H, H-2, H-3'), 3.55 (dd, *J* = 12.0, 4.7 Hz, 1H, H-1a), 3.45 (t, *J* = 6.2 Hz, 2H, H_2-5"), 3.40 – 3.32 (m, 2H, H-3, H-1"a), 3.26 (d, *J* = 9.7 Hz, 1H, H-5), 3.15 (td, *J* = 12.5, 5.1 Hz, 1H, H-1"b), 3.08 (s, 2H, H_2-6''), 3.04 (t, *J* = 11.8 Hz, 1H, H-1b), 1.88 – 1.71 (m, 2H, H_2-2"), 1.71 – 1.62 (m, 2H, H_2-4"), 1.50 – 1.43 (m, 2H, H_2-3"), 0.91 (s, 9H, H_3-8'', H_3-9'', H_3-10''). ^{13}C NMR (100 MHz, MeOD) δ 100.0 (C-1'), 82.6 (C-6''), 78.2 (C-3), 72.8 (C-5'), 72.1 (C-5"), 71.3 (C-2'), 70.8 (C-4), 70.0 (C-4'), 69.0 (C-3'), 68.0 (C-2), 66.2 (C-5), 62.5 (C-6), 60.3 (C-6'), 55.1 (C-1), 54.4 (C-1"), 32.9 (C-7''), 30.2 (C-4"), 27.1 (C_3-8'', C_3-9'', C_3-10''), 24.5 (C-3"), 24.0 (C-2"). $[\alpha]^{20}_D$ = +43.8 (c = 0.26, MeOH). IR/cm^{-1}: 3329, 2951, 2864, 1372, 1427, 1358, 1202, 1134, 1080, 1040. HRMS: found 482.29552 $[C_{22}H_{43}NO_{10}+H]^+$, calculated for $[C_{22}H_{43}NO_{10}+H]^+$ 482.29597.

2,3,6-Tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-*N*-butyl-1-deoxynojirimycin (18):



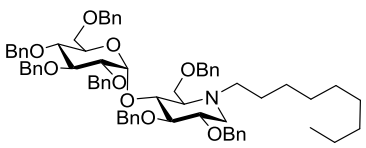
Protected *Malto*-DNJ (0.19 g, 0.2 mmol) was subjected to the general procedure C to generate **18** (0.12 g, 0.12 mmol) in a yield of 66%. R_F = 0.40 (4:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.09 (m, 35H, H_{Ar} Bn), 5.74 (d, *J* = 3.4 Hz, 1H, H-1), 5.00 – 4.26 (m, 14H, 7 x CH_2 Bn), 4.10 (t, *J* = 8.2 Hz, 1H, H-4), 3.98 (t, *J* = 9.3 Hz, 1H, H-3'), 3.80 (t, *J* = 9.6 Hz, 1H, H-5'), 3.76 – 3.58 (m, 5H, H-2, H-3, H-4', H-6a, H-6'a), 3.55 – 3.50 (m, 3H, H-2', H-6b, H-6'b), 3.08 (dd, *J* = 11.1, 4.7 Hz, 1H, H-1a), 2.57 – 2.50 (m, 3H, H_2-1", H-5), 2.33 (t, *J* = 10.7 Hz, 1H, H-1b), 1.30 (m, 2H, H_2-2"), 1.15 – 1.05 (m, 2H, H_2-3"), 0.82 (t, *J* = 7.3 Hz, 3H, H_3-4"). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.1 – 137.8 (7 x C_q Bn), 128.4 – 126.8 (CH_{Ar} Bn), 95.9 (C-1'), 86.3 (C-3), 82.2 (C-3'), 79.7 (C-2'), 78.6 (C-2), 77.7 (C-4'), 75.6 – 72.4 (7 x CH_2 Bn), 72.3 (C-4), 70.9 (C-5'), 68.2 (C-6), 65.9 (C-6'), 63.1 (C-5), 53.4 (C-1), 52.4 (C-1"), 26.4 (C-2"), 20.6 (C-3"), 14.1 (C-4"). $[\alpha]^{20}_D$ = +15.6 (c = 1.0, $CHCl_3$). IR/cm^{-1}: 3063, 3030, 2922, 2964, 1497, 1453, 1363, 1092, 1073, 1028. HRMS: found 1012.53472 $[C_{65}H_{74}NO_9+H]^+$, calculated for $[C_{65}H_{74}NO_9+H]^+$ 1012.53581.

4-*O*-(α-D-Glucopyranosyl)-*N*-butyl-1-deoxynojirimycin (19):



Malto-DNJ (**18**, 0.19 g, 0.2 mmol) was subjected to the general procedure C to generate **19** (26.1 mg, 0.07 mmol) as a white solid in 58% yield. ^{1}H-NMR (400 MHz, MeOD) δ 5.13 (d, *J* = 3.8 Hz, 1H, H-1'), 3.92 (dd, *J* = 12.2, 2.4 Hz, 1H, H-6a), 3.88 (dd, *J* = 12.2, 2.1 Hz, 1H, H-6b), 3.84 (dd, *J* = 11.6, 2.1 Hz, 1H, H-6a'), 3.74 (ddd, *J* = 9.8, 5.9, 2.0 Hz, 1H, H-5'), 3.66 (dd, *J* = 11.6, 6.0 Hz, 1H, H-6b'), 3.63 (t, *J* = 9.3 Hz, 1H, H-3'), 3.52 (t, *J* = 9.2 Hz, 1H, H-4), 3.51 (dd, *J* = 9.8, 4.9 Hz, 1H, H-2), 3.47 (dd, *J* = 9.7, 3.8 Hz, 1H, H-2'), 3.37 (t, *J* =9.1 Hz, 1H, H-3), 3.27 (dd, *J* = 9.9, 9.0 Hz, 1H, H-4'), 2.97 (dd, *J* = 11.0, 4.7 Hz, 1H, H-1a), 2.79 (m, 1H, H-1''a), 2.63 (m, 1H, H-1''b), 2.20 (dd, *J* = 11.3, 1.7 Hz, 1H, H-5), 2.19 (m, 1H, H-1b), 1.49 – 1.42 (m, 2H, H_2-2''), 1.35 – 1.29 (m, 2H, H_2-3''), 0.95 (t, *J* = 7.3 Hz, 3H, H_3-4''). ^{13}C NMR (100 MHz, MeOD) δ 103.5 (C-1'), 84.0 (C-2), 80.4 (C-3), 75.1 (C-3'), 74.8 (C-5'), 74.3 (C-2'), 71.6 (C-4'), 70.2 (C-4), 66.1 (C-5), 62.8 (C-6'), 58.5 (C-6), 57.5 (C-1), 53.4 (C-1"), 27.3 (C-2"), 21.8 (C-3"), 14.4 (C-4"). $[\alpha]^{20}_D$ = +42.1 (c = 0.76, MeOH). IR/cm^{-1}: 3309, 2961, 2932, 2479, 1636, 1456, 1373, 1146, 1076, 1034. HRMS: found 382.20730 $[C_{16}H_{31}NO_9+H]^+$, calculated for $[C_{16}H_{31}NO_9+H]^+$ 382.20716.

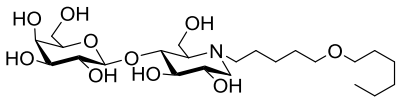
2,3,6-Tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucosepyranosyl)-*N*-nonyl-1-deoxynojirimycin (20).



Protected *malto*-DNJ (0.19 g, 0.2 mmol) was subjected to the general procedure C to generate **20** (0.13 g, 0.12 mmol) in a yield of 66% (0.133 g, 0.123 mmol). R_F = 0.66 (4:1,

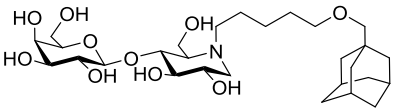
PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.10 (m, 35H, H_{Ar} Bn), 5.75 (d, *J* = 3.3 Hz, 1H, H-1), 5.01 – 4.26 (m, 14H, 7 x CH_2 Bn), 4.11 (t, *J* = 8.2 Hz, 1H, H-4), 3.99 (t, *J* = 9.2 Hz, 1H, H-3'), 3.80 (t, *J* = 9.2 Hz, 1H, H-5'), 3.76 – 3.58 (m, 5H, H-2, H-3, H-4', H-6a, H-6'a), 3.55 – 3.50 (m, 3H, H-2', H-6b, H-6'b), 3.08 (dd, *J* = 11.1, 4.7 Hz, 1H, H-1a), 2.57 – 2.50 (m, 3H, H_2-1'', H-5), 2.33 (t, *J* = 10.7 Hz, 1H, H-1b), 1.47-1.13 (m, 12H, H_2-2'' – H_2-7''), 1.12 – 1.02 (m, 2H, H_2-8''), 0.88 (t, *J* = 8.1, Hz, 3H, H_3-9''). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.1 – 137.8 (C_q Bn), 128.4 – 126.8 (CH_{Ar} Bn), 95.8 (C-1'), 86.3 (C-3), 82.1 (C-3'), 79.7 (C-2'), 78.6 (C-2), 77.7 (C-4'), 75.6 – 72.4 (7 x CH_2 Bn), 72.1 (C-4), 70 .9 (C-5'), 68.2 (C-6), 65.8 (C-6'), 63.0 (C-5), 53.4 (C-1), 32.0, 30.0, 29.6, 29.6, 29.3, 29.2, 27.4, 24.1, 22.8 (C-2'' – C-8''), 14.2 (C-9''). $[\alpha]^{20}_D$ = +16.0 (c = 1.02, $CHCl_3$). IR/cm^{-1}: 2954, 2925, 2853, 1539, 1506, 1093, 1073, 1028.

4-*O*-(β-D-Galactopyranosyl)-*N*-[5-(hexyloxy)pentyl]-1-deoxynojirimycin (21):



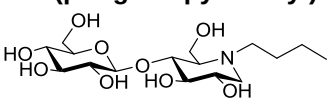
Lacto-DNJ was subjected to the general procedure A to generate **21** (5.6 mg, 0.01 mmol) in a yield of 11%. ^{1}H NMR (600 MHz, MeOD) δ 4.54 (d, *J* = 7.7 Hz, 1H, H-1'), 4.42 (d, *J* = 13.0 Hz, 1H, H-6a), 3.99 (d, *J* = 13.0 Hz, 1H, H-6b), 3.92 (dd, *J* = 3.3, 1.0 Hz, 1H, H-4'), 3.92 – 3.87 (m, 1H, H-4), 3.88 (dd, *J* = 11.5, 7.7 Hz, 1H, H-6'a), 3.86 – 3.83 (m, 1H, H-3), 3.81 (dd, *J* = 11.4, 4.4 Hz, 1H, H-6'b), 3.70 (q, *J* = 7.0 Hz, 1H, H-5'), 3.68 (dd, *J* = 12.3, 7.7 Hz, 1H, H-2'), 3.64 (t, *J* = 9.2 Hz, 1H, H-2), 3.59 (dd, *J* = 9.7, 3.3 Hz, 1H, H-3'), 3.55 (t, *J* = 6.2 Hz, 2H, H_2-5''), 3.55 – 3.51 (m, 1H, H-1a), 3.52 (t, *J* = 6.6 Hz, 2H, H_2-6''), 3.49 – 3.45 (m, 1H, H-1''a). 3.36 (d, *J* = 10.0 Hz, 1H, H-5), 3.33 – 3.26 (m, 1H, H-1''b), 3.13 (t, *J* = 11.7 Hz, 1H, H-1b), 1.95 – 1.80 (m, 2H, H_2-2''), 1.76 – 1.72 (m, 2H, H_2-4''), 1.68 – 1.62 (m, 2H, H_2-7''), 1.62 – 1.52 (m, 2H, H_2-3''), 1.49 – 1.36 (m, 6H, H_2-8'', H_2-9'', H_2-10''), 1.00 (t, *J* = 6.9 Hz, 3H, H_3-11''). ^{13}C NMR (150 MHz, MeOD) δ 106.1 (C-1'), 78.8 (C-4), 78.2 (C-5), 77.3 (C-2), 75.7 (C-3'), 73.4 (C-2'), 72.9 (C-6''), 72.2 (C-5''), 71.1 (C-4'), 68.4 (C-3), 67.1 (C-5), 63.4 (C-6'), 55.3 (C-1), 55.1 (C-1''), 55.1 (C-6), 33.7 (C-9''), 31.6 (C-7''), 31.0 (C-4''), 27.8 (C-8''), 25.3 (C-3''), 24.8 (C-2''), 24.5 (C-10''), 15.3 (C-11''). $[\alpha]^{20}_D$ = -4.0 (c = 0.2, MeOH). IR/cm^{-1}: 3395, 2956, 2872, 1670, 1435, 1201, 1142, 1080, 1047. HRMS: found 496.31127 $[C_{23}H_{45}NO_{10}+H]^+$, calculated for $[C_{23}H_{45}NO_{10}+H]^+$ 496.31162.

4-(β-D-Galactopyranosyl)-*N*-[5-(adamantan-1-yl-methoxy)-pentyl]-1-deoxynojirimycin (22):



Lacto-DNJ (**3**) was subjected to the general procedure A to generate **22** (6.72 mg, 0.01 mmol) in a yield of 12%. ^{1}H NMR (400 MHz, MeOD) δ 4.54 (d, *J* = 7.7 Hz, 1H, H-1'), 4.42 (d, *J* = 12.9 Hz, 1H, H-6a), 3.99 (d, *J* = 12.3 Hz, 1H, H-6b), 3.91 (dd, *J* = 3.3, 1.1 Hz, 1H, H-4'), 3.90 – 3.82 (m, 2H, H-4, H-3), 3.88 (dd, *J* = 11.4, 7.7 Hz, 1H, H-6'a), 3.80 (dd, *J* = 11.5, 4.4 Hz, 1H, H-6'b), 3.69 (ddd, *J* = 7.6, 4.3, 1.1 Hz, 1H, H-5'), 3.67 (dd, *J* = 8.3, 7.6 Hz, 1H, H-2'), 3.64 – 3.59 (m, 1H, H-2), 3.58 (dd, *J* = 9.8, 3.3 Hz, 1H, H-3'), 3.57 – 3.51 (m, 1H, H-1a), 3.51 (t, *J* = 6.1 Hz, 2H, H-5''), 3.49 – 3.45 (m, 1H, H-1''a), 3.37 – 3.26 (m, 2H, H-5, H-1''b), 3.13 (t, *J* = 11.7 Hz, 1H, H-1b), 3.07 (s, 2H, H_2-6''), 2.06 – 2.02 (m, 3H, 3 x CH ada), 1.96 – 1.69 (m, 10H, H_2-4'', 3 x CH_2 ada), 1.68 – 1.63 (m, 6H, 3 x CH_2 ada), 1.63 – 1.51 (m, 2H, H_2-3''). ^{13}C NMR (100 MHz, MeOD) δ 105.8 (C-1'), 84.0 (C-6''), 78.8 (C-4'), 78.2 (C-5'), 76.9 (C-2), 75.7 (C-3'), 73.4 (C-2'), 72.9 (C-5''), 71.1 (C-4), 68.4 (C-3), 67.1 (C-5), 63.4 (C-6'), 54.8 (C-6), 54.9 (C-1), 54.9 (C-1''), 41.7 (CH_2-ada), 39.2 (CH_2-ada), 36.0 (C_q-ada), 31.0 (C-2''), 30.6 (CH-ada), 27.3 (C-3''), 25.4 (C-4''). $[\alpha]^{20}_D$ = -17.0 (c = 0.2, MeOH). IR/cm^{-1}: 3391, 2903, 2849, 1674, 1435, 1204, 1136, 1082, 1053. HRMS: found 560.34253 $[C_{28}H_{49}NO_{10}+H]^+$, calculated for $[C_{28}H_{49}NO_{10}+H]^+$ 560.34292.

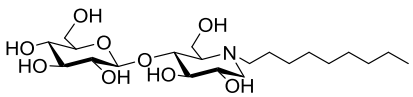
4-*O*-(β-D-glucopyranosyl)-*N*-butyl-1-deoxynojirimycin (23):



Cellibio-DNJ (**4**) was subjected to the general procedure A to generate **23** (6.5 mg, 0.02 mmol) in a yield of 17%. ^{1}H NMR (400

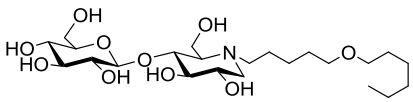
MHz, MeOD) δ 4.59 (d, *J* = 7.8 Hz, 1H, H-1'), 4.37 (dd, *J* = 12.9, 1.7 Hz, 1H, H-6a), 4.00 (dd, *J* = 12.9, 2.8 Hz, 1H, H-6b), 3.99 (dd, *J* = 11.8, 2.1 Hz, 1H, H-6'a), 3.87 (dd, *J* = 10.0, 9.0 Hz, 1H, H-4), 3.83 (ddd, *J* = 11.0, 9.1, 4.9 Hz, 1H, H-2), 3.75 (dd, *J* = 11.8, 6.0 Hz, 1H, H-6'b), 3.61 (t, *J* = 9.0 Hz, 1H, H-3), 3.53 – 3.33 (m, 6H, H-1a, H-1''a, H-2', H-3', H-4', H-5'), 3.30 – 3.18 (m, 2H, H-5, H-1''b), 3.03 (t, *J* = 11.5 Hz, 1H, H-1b), 1.87 – 1.71 (m, 2H, H_2-2''), 1.57 – 1.45 (m, 2H, H_2-3''), 1.10 (t, *J* = 7.4 Hz, 3H, H_3-4''). ^{13}C NMR (100 MHz, MeOD) δ 105.6 (C-1'), 79.6 (C-4), 79.2 (C-3'), 78.7 (C-5'), 77.4 (C-3), 75.8 (C-2'), 72.2 (C-4'), 68.8 (C-2), 67.1 (C-5), 63.3 (C-6'), 55.8 (C-6), 55.5 (C-1), 54.7 (C-1''), 27.2 (C-2''), 21.9 (C-3''), 14.8 (C-4''). $[\alpha]^{20}_D$ = -17.0 (c = 0.2, MeOH). HRMS: found 382.20752 $[C_{16}H_{31}NO_9+H]^+$, calculated for $[C_{16}H_{31}NO_9+H]^+$ 382.20716.

4-*O*-(β-D-Glucopyranosyl)-*N*-nonyl-1-deoxynojirimycin (24):



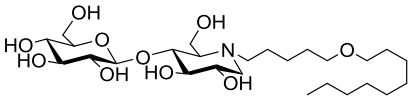
Cellobio-DNJ (**4**) was subjected to the general procedure A to generate **24** (3.6 mg, 0.01 mmol) in a yield of 8%. ^{1}H NMR (600 MHz, MeOD) δ 4.51 (d, *J* = 7.8 Hz, 1H, H-1'), 4.36 (d, *J* = 12.9 Hz, 1H, H-6a), 3.92 (dd, *J* = 11.8, 2.2 Hz, 1H, H-6'a), 3.90 (dd, *J* = 12.6, 2.4 Hz, 1H, H-6b), 3.81 (t, *J* = 9.7 Hz, 1H, H-4), 3.76 (td, *J* = 11.3, 5.3 Hz, 1H, H-2), 3.68 (dd, *J* = 11.8, 6.2 Hz, 1H, H-6'b), 3.55 (t, *J* = 9.1 Hz, 1H, H-3), 3.47 (dd, *J* = 12.2, 5.0 Hz, 1H, H-1a), 3.42 – 3.26 (m, 6H, H-1''a, H-2', H-3', H-4', H-5', H-5), 3.25 – 3.18 (m, 1H, H-1''b), 3.05 (t, *J* = 11.7 Hz, 1H, H-1b), 1.84 – 1.69 (m, 2H, H_2-2''), 1.50 – 1.26 (m, 12H, H_2-3'' – H_2-8''), 0.93 (t, *J* = 7.0, 3H, H_3-9''). ^{13}C NMR (150 MHz, MeOD) δ 104.4 (C-1'), 78.0 (C-5'), 77.8 (C-4), 77.5 (C-3'), 75.9 (C-3), 74.5 (C-2'), 70.9 (C-4'), 67.2 (C-2), 65.8 (C-5), 62.0 (C-6'), 53.9 (C-1''), 53.9 (C-1), 53.7 (C-6), 32.6, 30.1, 29.9, 29.8, 27.2, 23.7, 23.3 (C-2'' – C-8''), 14.0 (C-9''). $[\alpha]^{20}_D$ = +9.0 (c = 0.2, MeOH). IR/cm^{-1}: 3337, 2923, 1669, 1203, 1135, 1073. HRMS: found 452.28500 $[C_{21}H_{41}NO_9+H]^+$, calculated for $[C_{21}H_{41}NO_9+H]^+$ 452.28541.

4-*O*-(β-D-Glucopyranosyl)-*N*-[5-(hexyloxy)pentyl]-1-deoxynojirimycin (25):



Cellobio-DNJ (**4**) was subjected to the general procedure A to generate **25** (5.5 mg, 0.01 mmol) in a yield of 11%. ^{1}H NMR (600 MHz, MeOD) δ 4.58 (d, *J* = 7.8 Hz, 1H, H-1'), 4.42 (d, *J* = 13.0 Hz, 1H, H-6a), 3.99 (dd, *J* = 11.8, 2.2 Hz, 1H, H-6'a), 3.98 (d, *J* = 12.1 Hz, 1H, H-6b), 3.87 (t, *J* = 9.7 Hz, 1H, H-4), 3.83 (ddd, *J* = 11.1, 10.6, 4.9 Hz, 1H, H-2), 3.75 (dd, *J* = 11.9, 6.2 Hz, 1H, H-6'b), 3.55 (t, *J* = 6.3 Hz, 2H, H_2-6''), 3.55 – 3.51 (m, 1H, H-1a), 3.52 (t, *J* = 6.6 Hz, 2H, H_2-5''), 3.49 – 3.44 (m, 1H, H-1''a), 3.46 (t, *J* = 9.0 Hz, 1H, H-3'), 3.45 (ddd, *J* = 9.1, 6.2, 2.3 Hz, 1H, H-5'), 3.39 (t, *J* = 9.4 Hz, 1H, H-4'), 3.36 (dd, *J* = 9.1, 7.9 Hz, 1H, H-2'), 3.35 – 3.26 (m, 2H, H-5, H-1''b), 3.11 (t, *J* = 11.4 Hz, 1H, H-1b), 1.94 – 1.77 (m, 2H, H_2-2''), 1.78 – 1.71 (m, 2H, H_2-4''), 1.67 – 1.63 (m, 2H, H_2-7''), 1.60 – 1.53 (m, 2H, H_2-3''), 1.48 – 1.34 (m, 6H, H_2-8'', H_2-9'', H_2-10''), 1.00 (t, *J* = 6.9 Hz, 3H, H_3-11''). ^{13}C NMR (150 MHz, MeOD) δ 105.6 (C-1'), 79.2 (C-5'), 78.8 (C-4, C-3'), 77.2 (C-3), 75.8 (C-2'), 73.0 (C-5''), 72.2 (C-6''), 72.1(C-4'), 68.5(C-2), 67.1 (C-5), 63.3 (C-6'), 55.3 (C-1), 55.0 (C-1'), 55.0 (C-6), 33.7 (C-9''), 31.6 (C-7''), 31.0 (C-4''), 27.8 (C-8''), 25.4 (C-3''), 24.8 (C-2''), 24.6 (C-10''), 15.3 (C-11''). $[\alpha]^{20}_D$ = +0.3 (c = 1.0, MeOH). IR/cm^{-1}: 3298, 2874, 2511, 1635, 1456, 1317, 1015. HRMS: found 496.31124 $[C_{23}H_{45}NO_{10}+H]^+$, calculated for $[C_{23}H_{45}NO_{10}+H]^+$ 496.31162.

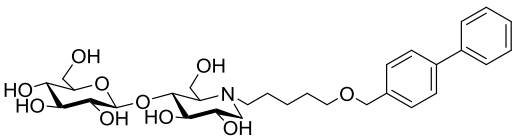
4-*O*-(β-D-Glucopyranosyl)-*N*-[5-(nonyloxy)pentyl]-1-deoxynojirimycin (26):



Cellobio-DNJ (**4**) was subjected to the general procedure A to generate **26** (4.8 mg, 0.01 mmol) in a yield of 9%. ^{1}H NMR (600 MHz, MeOD) δ 4.51 (d, *J* = 7.8 Hz, 1H, H-1'), 4.34 (d, *J* = 12.6 Hz, 1H, H-6a), 3.92 (dd, *J* = 11.8, 2.3 Hz, 1H, H-6'a), 3.84 – 3.73 (m, 2H, H-4, H-2), 3.68 (dd, *J* = 11.8, 6.2 Hz, 1H, H-6'b), 3.54 (t, *J* = 8.9 Hz, 1H, H-3), 3.48 (t, *J* = 6.3 Hz, 2H, H_2-5''), 3.45 (t, *J* = 6.6 Hz, 2H, H_2-6''), 3.49 – 3.45 (m, 1H, H-1a), 3.40 – 3.18 (m, 7H, H-1''a, H-1''b, H-2', H-3', H-4', H-5', H-5), 1.85 – 1.73 (m, 2H, H_2-2''), 1.71 – 1.63 (m, 2H, H_2-4''), 1.61 – 1.55 (m, 2H, H_2-7''), 1.54 – 1.44 (m, 2H, H_2-3''), 1.42 – 1.26 (m, 12H,

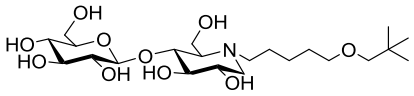
H_2-8'' – H_2-13''), 0.92 (t, *J* = 7.0 Hz, 3H, H_3-14''). ^{13}C NMR (150 MHz, MeOD) δ 103.4 (C-1'), 77.0 (C-4), 76.8 (C-5'), 76.5 (C-3'), 75.2 (C-3), 73.5 (C-2'), 70.7 (C-6''), 70.0 (C-5''), 69.9 (C-4'), 61.0 (C-2), 53.1 (C-6'), 52.9 (C-1), 52.7 (C-6), 48.0 (C-1''), 31.6, 29.4, 29.3, 29.2, 29.0, 28.8, 25.9, 23.1, 22.5, 22.3, 13.0 (C-2'' – 4'', C-7'' – C-14''). $[\alpha]^{20}_D$ = -7.0 (c = 0.1, MeOH). IR/cm^{-1}: 3383, 2933, 1705, 1203, 1142. HRMS: found 538.35812 $[C_{26}H_{51}NO_{10}+H]^+$, calculated for $[C_{26}H_{51}NO_{10}+H]^+$ 538.35857.

4-*O*-(β-D-Glucopyranosyl)-*N*-[(biphenyl-4-yl-methoxy)-pentyl]-1-deoxynojirimycin (27):



Cellobio-DNJ (**4**) was subjected to the general procedure A and generated **27** (8.7 mg, 0.02 mmol) in a yield of 15%. ^{1}H NMR (600 MHz, MeOD) δ 7.66 – 7.29 (m, 9H, H_{Ar} BiPh), 4.57 (s, 2H, H_2-6''), 4.50 (d, *J* = 7.9 Hz, 1H, H-1'), 4.34 (d, *J* = 12.9 Hz, 1H, H-6a), 3.91 (dd, *J* = 11.8, 2.2 Hz, 1H, H-6'a), 3.90 (d, *J* = 13.5 Hz, 1H, H-6b), 3.82 – 3.73 (m, 2H, H-2, H-4), 3.68 (dd, *J* = 11.8, 6.2 Hz, 1H, H-6'b), 3.59 (t, *J* = 6.2 Hz, 2H, H_2-5''), 3.56 – 3.51 (m, 1H, H-3), 3.49 – 3.43 (m, 1H, H-1a), 3.43 – 3.16 (m, 7H, H-1''a, H-1''b, H-2', H-3', H-4', H-5', H-5), 3.02 (t, *J* = 11.7 Hz, 1H, H-1b), 1.86 – 1.77 (m, 2H, H_2-2''), 1.76 – 1.70 (m, 2H, H_2-3''), 1.60 – 1.48 (m, 2H, H_2-4''). ^{13}C NMR (150 MHz, MeOD) δ 141.7 – 127.6 (C_{Ar} BiPh), 104.3 (C-1'), 78.0 (C-4), 77.7 (C-5'), 77.5 (C-3'), 76.0 (C-3), 74.5 (C-2'), 73.3 (C-6''), 70.9 (C-4'), 70.5 (C-5''), 67.3 (C-2), 65.8 (C-5), 62.0 (C-6), 54.3 (C-1), 54.1 (C-6), 53.8 (C-1''), 29.7 (C-4''), 24.2 (C-3''), 23.5 (C-2''). $[\alpha]^{20}_D$ = +0.5 (c = 0.2, MeOH). IR/cm^{-1}: 3368, 2318, 1674, 1205, 1134, 1080. HRMS: found 578.29406 $[C_{30}H_{43}NO_{10}+H]^+$, calculated for $[C_{30}H_{43}NO_{10}+H]^+$ 578.29597.

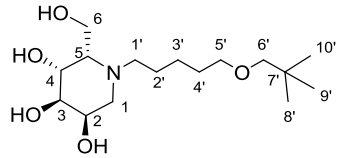
4-*O*-(β-D-Glucopyranosyl)-*N*-[5-(3,3-dimethyl-1-propyloxy)pentyl]-1-deoxynojirimycin (28):



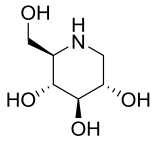
Cellobio-DNJ (**4**) was subjected to the general procedure A and generated **28** (4.8 mg, 0.01 mmol) in a yield of 10%. ^{1}H NMR (400 MHz, MeOD) δ 4.58 (d, *J* = 7.8 Hz, 1H, H-1'), 4.30 (dd, *J* = 12.4, 1.7 Hz, 1H, H-6'a), 3.98 (dd, *J* = 12.1, 4.5 Hz, 1H, H-6a), 3.98 (d, *J* = 12.0 Hz, 1H, H-6'b), 3.81 (t, *J* = 9.6 Hz, 1H, H-4), 3.81 – 3.73 (m, 1H, H-2), 3.75 (dd, *J* = 11.9, 6.0 Hz, 1H, H-6b), 3.53 (t, *J* = 9.6 Hz, 2H, H_2-5''), 3.50 – 3.45 (m, 2H, H-3, H-5'), 3.45 – 3.41 (m, 2H, H-4', H-2'), 3.35 (dd, *J* = 9.0, 7.8 Hz, 1H, H-1a), 3.29 – 3.19 (m, 1H, H-1''a), 3.17 (s, 2H, H_2-6''), 3.14 – 3.03 (m, 1H, H-1''b), 3.00 (d, *J* = 9.3 Hz, 1H, H-5), 2.81 (t, *J* = 11.5 Hz, 1H, H-1b), 1.86 – 1.68 (m, 4H, H_2-2'', H_2-3''), 1.63 – 1.48 (m, 2H, H_2-4''), 1.00 (s, 9H, H_3-8'', H_3-9'', H_3-10''). ^{13}C NMR (100 MHz, MeOD) δ 105.6 (C-1'), 83.4 (C-6''), 80.6 (C-4), 79.1 (C-5'), 78.8 (C-3), 78.0 (C-3'), 75.9 (C-2'), 73.0 (C-5''), 72.2 (C-4'), 69.6 (C-2), 67.1 (C-5), 63.3 (C-6), 56.2 (C-6'), 54.7 (C-1), 54.1 (C-1''), 33.8 (C-7''), 31.2 (C-2''), 28.0 (C-8'', 9'', 10''), 25.7 (C-4''), 25.3 (C-3''). $[\alpha]^{20}_D$ = +0.5 (c = 1.0, MeOH). IR/cm^{-1}: 3308, 2980, 2875, 2349, 1635, 1080, 1031. HRMS: found 482.29552 $[C_{22}H_{43}NO_{10}+H]^+$, calculated for $[C_{22}H_{43}NO_{10}+H]^+$ 482.29597.

Synthesis of *N*-Alkylated DNJ and DNJ congeners

***Figure 19**: Proton and carbon NMR numbering of iminosugars*

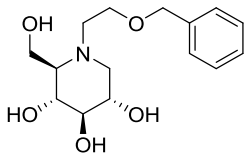


1-Deoxynojirimycin (85):



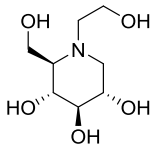
^{1}H NMR (400 MHz, MeOD) δ 3.92 (dd, *J* = 10.9, 3.1 Hz, 1H, H-6a), 3.67 (dd, *J* = 10.9, 6.5 Hz, 1H, H-6b), 3.49 (ddd, *J* = 10.6, 8.7, 5.1 Hz, 1H, H-2), 3.28 (t, *J* = 8.1 Hz, 1H, H-3), 3.24 (t, *J* = 9.1 Hz, 1H, H-4), 3.18 (dd, *J* = 12.1, 5.1 Hz, 1H, H-1a), 2.54 (ddd, *J* = 9.4, 6.4, 3.1 Hz, 1H, H-5), 2.52 (dd, *J* = 12.1, 10.7 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, MeOD) δ 81.5 (C-3), 74.2 (C-4), 73.5 (C-2), 64.0 (C-6), 63.7 (C-5), 51.9 (C-1).

***N*-Benzyloxyethyl-1-deoxynojirimycin (90):**



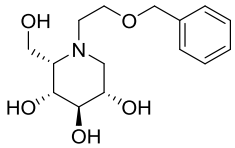
DNJ (**85**) was subjected to the general procedure A and generated **90** (12.4 mg, 0.04 mmol) in a yield of 38%. ^{1}H NMR (400 MHz, MeOD) δ 7.45 – 7.33 (m, 5H, H_{Ar} Bn), 4.61 (s, 2H, CH_2 Bn), 4.02 (dd, *J* = 12.1, 2.7 Hz, 1H, H-6a), 3.92 (dd, *J* = 12.1, 2.8 Hz, 1H, H-6b), 3.73 – 3.69 (m, 2H, H_2-2'), 3.55 (ddd, *J* = 10.5, 9.1, 4.8 Hz, 1H, H-2), 3.45 (t, *J* = 9.3 Hz, 1H, H-4), 3.23 (t, *J* = 9.1 Hz, 1H, H-3), 3.19 – 3.13 (m, 1H, H-1'a), 3.15 (dd, *J* = 10.5, 5.1 Hz, 1H, H-1a), 2.84 (dt, *J* = 14.5, 4.6 Hz, 1H, H-1'b), 2.38 (dd, *J* = 11.3, 10.5 Hz, 1H, H-1b), 2.30 (dt, *J* = 9.5, 2.7 Hz, 1H, H-5). ^{13}C NMR (100 MHz, MeOD) δ 131.3 – 129.6 (C_{Ar}), 81.3 (C-3), 75.0 (CH_2 Bn), 72.6 (C-4), 71.5 (C-2), 69.4 (C-2'), 68.5 (C-5), 60.2 (C-6), 59.3 (C-1), 53.4 (C-1'). HRMS: found 298.16505 $[C_{15}H_{23}NO_5+H]^+$, calculated for $[C_{15}H_{23}NO_5+H]^+$ 298.16490.

***N*-Hydroxyethyl-1-deoxynojirimycin (90a):**



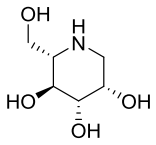
90 (60 mg, 0.2 mmol) was dissolved in 5 mL ethanol and the pH of the solvent was adjusted to 2 with aqueous HCl (1M). After the solution was flushed with argon (3 x), a catalytic amount of Pd/C (10%) was added. The reaction mixture was exposed to H_2 atmosphere (3 bar) for 18 hours. TLC analysis showed completely consumption of **90.** 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 give **90a** as a colorless oil in a of yield 65% (27 mg, 0.13 mmol). ^{1}H NMR (400 MHz, MeOD) δ 4.21 (dd, *J* = 12.6, 0.9 Hz, 1H, H-6a), 4.08 (dd, *J* = 12.6, 2.9 Hz, 1H, H-6b), 4.05 (t, *J* = 5.1 Hz, 2H, H_2-2'), 3.82 (ddd, *J* = 11.2, 9.3, 4.9 Hz, 1H, H-2), 3.74 (dd, *J* = 12.1, 4.9 Hz, 1H, H-1a), 3.71 (dd, *J* = 10.4, 9.2 Hz, 1H, H-4), 3.70 – 3.63 (m, 1H, H-1'a), 3.47 (t, *J* = 9.2 Hz, 1H, H-3), 3.46 – 3.41 (m, 1H, H-1'a), 3.26 (d, *J* = 10.9 Hz, 1H, H-5), 3.20 (t, *J* = 11.7 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, MeOD) δ 79.0 (C-3), 69.7 (C-4), 69.3 (C-5), 68.6 (C-2), 57.7 (C-2'), 57.0 (C-1'), 56.5 (C-1), 56.0 (C-6). $[\alpha]^{20}_D$ = -42.0 (c = 0.2, MeOH). HRMS: found 208.11795 $[C_8H_{17}NO_5+H]^+$, calculated for $[C_8H_{17}NO_5+H]^+$ 208.11795.

***N*-Benzyloxyethyl-L-*ido*-1-deoxynojimycin (97):**



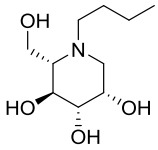
L-*ido*-DNJ was subjected to the general procedure A and generated **97** (21 mg, 0.07 mmol) in a yield of 12%. ^{1}H NMR (400 MHz, MeOD) δ 7.50 – 7.29 (m, 5H, H_{Ar} Bn), 4.62 (s, 2H, CH_2 Bn), 4.03 (d, *J* =11.2, 6.4 Hz, 1H, H-6a), 3.87 (dd, *J* = 10.8, 6.4 Hz, 1H, H-6b), 3.80 (dd, *J* = 8.9, 5.3 Hz, 1H, H-4), 3.70 (t, *J* = 5.6 Hz, 2H, H_2-2'), 3.63 (ddd, *J* = 12.7, 8.9, 5.1 Hz, 1H, H-2), 3.45 (t, *J* = 8.5 Hz, 1H, H-3), 3.17 (m, *J* = 5.6 Hz, 1H, H-5), 3.11 (t, *J* = 5.6 Hz, 1H, H-1'a), 3.04 (t, *J* = 5.6 Hz, 1H, H-1'b), 2.97 (dd, *J* = 12.7, 4.9 Hz, 1H, H-1a), 2.75 (dd, *J* = 12.6, 9.7 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, MeOD) δ 140.5 – 129.0 (CH_{Ar} Bn), 76.7 (C-3), 75.0 (CH_2 Bn), 73.3 (C-4), 71.9 (C-2), 70.7 (C-2'), 65.7 (C-5), 58.8 (C-6), 56.2 (C-1'), 53.7 (C-1). $[\alpha]^{20}_D$ = -18.0 (c = 0.5, MeOH). IR/cm^{-1}: 3331, 2864, 1653, 1456, 1362, 1059, 1027. HRMS: found 298.16512 $[C_{15}H_{23}NO_5+H]^+$, calculated for $[C_{15}H_{23}NO_5+H]^+$ 298.16490.

L-*Manno*-1-deoxynojimycin (129):



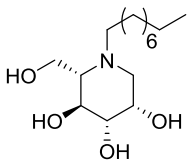
2,3,4-Tri-*O*-benzyl-L-*manno*-1-deoxynojimycin (0.84 g, 1.94 mmol) was dissolved in ethanol (100 mL) and pH of the solution was adjusted to 2 with aqueous HCl (1M). The solvent was flushed with argon (3 x), a catalytic amount of Pd/C (10%) was added, and the reaction mixture was exposed to H_2 atmosphere (2 bar) for 18 hours. After TLC analysis showed completely consumption of the starting compound, 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 give **129** (0.19 g, 1.14 mmol) in a yield of 59%**.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.12 (s, 1H, H-2), 4.02 (d, *J* = 12.0 Hz, 1H, H-6a), 3.86 (d, *J* = 12.4 Hz, 1H, H-6b), 3.84 (d, *J* = 10.8 Hz, 1H, H-4), 3.63 (d, *J* = 9.6 Hz, 1H, H-3), 3.36 (d, *J* = 13.2 Hz, 1H, H-1a), 3.25 (d, *J* = 13.6 Hz, 1H, H-1b), 3.12 – 3.07 (m, 1H, H-5). ^{13}C NMR (100 MHz, $CDCl_3$) δ 73.0 (C-3), 66.2 (C-4), 66.2 (C-2), 61.0 (C-5), 58.2 (C-6), 34.1 (C-1). $[\alpha]^{20}_D$ = +4.3 (c = 1.0, MeOH). IR/cm^{-1}: 3348, 2924, 1653, 1448, 1144, 1081, 1047. HRMS: found 164.09167 $[C_6H_{13}NO_4+H]^+$, calculated for $[C_6H_{13}NO_4+H]^+$ 164.09173.

***N*-Butyl- L-*manno*-1-deoxynojimycin (130):**



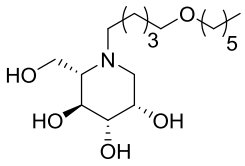
129 was subjected to the general procedure A and generated **130** (18 mg, 0.04 mmol) in a yield of 42%. ^{1}H NMR (400 MHz, MeOD) δ 4.21 (ddd, *J* = 3.9, 3.2, 1.5 Hz, H-2), 4.17 (dd, *J* = 12.7, 2.9 Hz, 1H, H-6a), 4.05 (dd, *J* = 12.9, 2.8 Hz, 1H, H-6b), 4.04 (t, *J* = 9.5 Hz, 1H, H-4), 3.66 (dd, *J* = 9.2, 3.0 Hz, 1H, H-3), 3.55 (dd, *J* = 12.9, 3.7 Hz, 1H, H-1a), 3.47 (d, *J* = 13.0 Hz, 1H, H-1b), 3.44 – 3.35 (m, 2H, H_2-1'), 3.14 (dt, *J* = 9.9, 3.0 Hz, 1H, H-5), 1.94 – 1.72 (m, 2H, H_2-2'), 1.54 – 1.50 (m, 2H, H_2-3'), 1.10 (t, *J* = 7.4 Hz, 3H, H_3-4'). ^{13}C NMR (100 MHz, MeOD) δ 75.0 (C-3), 68.6 (C-5), 68.0 (C-2), 67.8 (C-4), 56.9 (C-6), 56.9 (C-1), 55.2 (C-1'), 26.6 (C-2'), 21.8 (C-3'), 14.8 (C-4'). $[\alpha]^{20}_D$ = -7.2 (c = 1.0, MeOH). IR/cm^{-1}: 3244, 2954, 2872, 2619, 1635, 1435, 1259, 1076, 1020. HRMS: found 220.15434 $[C_{10}H_{21}NO_4+H]^+$, calculated for $[C_{10}H_{21}NO_4+H]^+$ 220.15433.

***N*-Nonyl- L-*manno*-1-deoxynojimycin (131):**



129 was subjected to the general procedure A and generated **131** (10 mg, 0.03 mmol) in a yield of 17%. ^{1}H NMR (400 MHz, MeOD) δ 4.00 (dd, *J* = 11.8, 2.6 Hz, 1H, H-6a), 3.96 – 3.92 (m, 1H, H-2), 3.95 (dd, *J* = 11.7, 2.9 Hz, 1H, H-6b), 3.78 (t, *J* = 9.1 Hz, 1H, H-4), 3.42 (dd, *J* = 9.0, 3.4 Hz, 1H, H-3), 3.11 (dd, *J* = 12.3, 3.9 Hz, 1H, H-1a), 2.95 – 2.83 (m, 1H, H-1'a), 2.80 – 2.70 (m, 1H, H-1'b), 2.66 (d, *J* = 12.3 Hz, 1H, H-1b), 2.32 – 2.28 (m, 1H, H-5), 1.65 – 1.51 (m, 2H, H_2-2'), 1.47 – 1.32 (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 77.2 (C-3), 70.2 (C-4), 70.2 (C-2), 67.9 (C-5), 59.7 (C-6), 57.3 (C-1), 54.8 (C-1'), 33.9, 31.6, 31.5, 31.3, 29.4, 26.0, 24.6 (C-2' – C-8'), 15.3 (C-9'). $[\alpha]^{20}_D$ = +6.0 (c = 1.0, MeOH). IR/cm^{-1}: 3392, 2924, 2857, 2503, 1635, 1435, 1273, 1082. HRMS: found 290.23291 $[C_{15}H_{31}NO_4+H]^+$, calculated for $[C_{15}H_{31}NO_4+H]^+$ 290.23258.

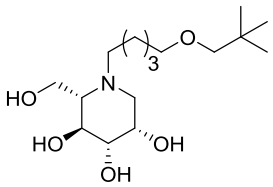
***N*-[5-(Hexyloxy)pentyl]- L-*manno*-1-deoxynojimycin (132)**



129 was subjected to the general procedure A and generated **132** (27 mg, 0.08 mmol) in a yield of 41%. ^{1}H NMR (400 MHz, MeOD) δ 3.92 (dd, *J* = 4.7, 2.7 Hz, 2H, H_2-6), 3.90 – 3.86 (m, 1H, H-2), 3.72 (t, *J* = 9.1 Hz, 1H, H-4), 3.36 (dd, *J* = 8.8, 3.1 Hz, 1H, H-3), 3.06 (dd, *J* = 12.4, 3.9 Hz, 1H, H-1a), 2.92 – 2.78 (m, 1H, H-1'a), 2.75 – 2.65 (m, 1H, H-1'b), 2.61 (d, *J* = 12.4 Hz, 1H, H-1b), 2.25 (d, *J* = 9.0 Hz, 1H, H-5), 1.74 – 1.27 (m, 14H, H_2-2', H_2-3', H_2-4', H_2-7', H_2-8', H_2-9', H_2-10'), 0.93 (t, *J* = 7.1 Hz, 3H, H_3-11'). ^{13}C NMR (100 MHz, MeOD) δ 77.2 (C-3), 72.8 (C-6'), 72.6 (C-5'), 70.2 (C-2), 70.2 (C-4), 67.9 (C-5), 59.7 (C-6), 57.2 (C-1), 54.7 (C-1'), 33.7, 31.6, 31.4, 27.8, 26.0, 25.8, 24.6 (C-2' – C-4', C-7' – C-10'), 15.3 (C-11').

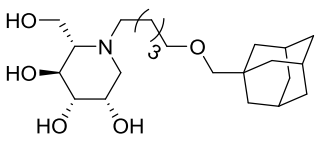
$[\alpha]^{20}_D$ = +31.5 (c = 1.0, MeOH). IR/cm^{-1}: 3392, 2932, 2867, 1684, 1456, 1373, 1099. HRMS: found 334.25936 $[C_{17}H_{35}NO_5+H]^+$, calculated for $[C_{17}H_{35}NO_5+H]^+$ 334.25880.

_N_-[5-(3,3-Dimethyl-1-propyloxy)pentyl]- L-_manno_-1-deoxynojimycin (133):



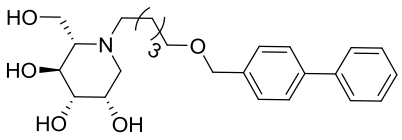
129 was subjected to the general procedure A and generated **133** (15 mg, 0.05 mmol) in a yield of 24%. ^{1}H NMR (400 MHz, MeOD) δ 4.00 (dd, *J* = 11.9, 2.8 Hz, 1H, H-6a), 3.96 (dd, *J* = 11.7, 2.9 Hz, 1H, H-6b), 3.95 – 3.92 (m, 1H, H-2), 3.78 (t, *J* = 9.1 Hz, 1H, H-4), 3.51 (t, *J* = 6.4 Hz, 2H, H-5'), 3.42 (dd, *J* = 8.5, 3.4 Hz, 1H, H-3), 3.16 (s, 2H, H_2-6'), 3.11 (dd, *J* = 12.4, 3.9 Hz, 1H, H-1a), 2.98 – 2.81 (m, 1H, H-1'a), 2.81 – 2.69 (m, 1H, H-1'b), 2.65 (d, *J* = 12.3 Hz, 1H, H-1b), 2.29 (d, *J* = 8.9 Hz, 1H, H-5), 1.73 – 1.66 (m, 2H, H_2-4'), 1.65 – 1.56 (m, 2H, H_2-2'), 1.51 – 1.37 (m, 2H, H_2-3'), 0.99 (s, 9H, H_3-8', H_3-9', H_3-10'). ^{13}C NMR (100 MHz, MeOD) δ 81.1 (C-6'), 75.0 (C-3), 71.0 (C-5'), 68.0 (C-2), 68.0 (C-4), 65.6 (C-5), 57.5 (C-6), 55.0 (C-1), 52.5 (C-1'), 31.5 (C-4'), 29.2 (C-7'), 25.7 (C-8',9',10'), 23.8 (C-3'), 23.5 (C-2'). $[\alpha]^{20}_D$ = +34.0 (c = 0.2, MeOH). IR/cm^{-1}: 3390, 2955, 2507, 1645, 1435, 1273, 1089. HRMS: found 320.24339 $[C_{16}H_{33}NO_5+H]^+$, calculated for $[C_{16}H_{33}NO_5+H]^+$ 320.24315.

_N_-[5-(Adamantan-1-yl-methoxy)pentyl]- L-_manno_-1-deoxynojimycin (84):



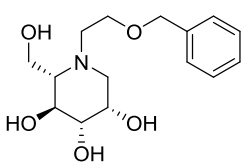
129 was subjected to the general procedure A and generated **84** (14 mg, 0.04 mmol) in a yield of 18%. ^{1}H NMR (600 MHz, MeOD) δ 4.22 – 4.19 (m, 1H, H-2), 4.16 (dd, *J* = 12.7, 3.3 Hz, 1H, H-6a), 4.05 (dd, *J* = 12.7, 2.9 Hz, 1H, H-6b), 4.02 (t, *J* = 9.3 Hz, 1H, H-4), 3.69 – 3.62 (m, 1H, H-3), 3.60 (t, *J* = 7.3 Hz, 2H, H_2-5'), 3.57 (s, 2H, H_2-6'), 3.53 (dd, *J* = 12.8, 4.0 Hz, 1H, H-1a), 3.47 – 3.41 (m, 3H, H_2-1', H-1b), 3.12 (br s, 1H, H-5), 2.07 – 1.98 (m, 3H, 3 x CH ada), 1.95 – 1.91 (m, 2H, H_2-2'), 1.87 – 1.80 (m, 3H, 3 x CH_2 ada), 1.80 – 1.70 (m, 7H, 3 x CH_2 ada, C-4'), 1.65 (d, *J* = 2.8 Hz, 6H, 3 x CH_2 ada), 1.46 (t, *J* = 7.4 Hz, 2H, H_2-3'). ^{13}C NMR (150 MHz, MeOD) δ 75.1 (C-3), 71.7 (C-6'), 68.8 (C-5'), 68.6 (C-5), 68.0 (C-2), 68.0 (C-4), 56.7 (C-6), 56.6 (C-1), 55.0 (C-1'), 45.7 (C-3'), 44.7 (CH_2 ada), 39.0 (CH_2 ada), 33.6 (C_q ada), 31.0 (CH ada), 28.7 (C-2'). IR/cm^{-1}: 3393, 2901, 2830, 1684, 1506, 1456, 1418, 1396, 1373, 1078. $[\alpha]^{20}_D$ = +13.8 (c = 0.5, MeOH). HRMS: found 398.28949 $[C_{22}H_{39}NO_5+H]^+$, calculated for $[C_{22}H_{39}NO_5+H]^+$ 398.29010.

_N_-[(Biphenyl-4-yl-methoxy)pentyl]- L-_manno_-1-deoxynojimycin (134):



129 was subjected to the general procedure A and generated **134** (15 mg, 0.04 mmol) in a yield of 18%. ^{1}H NMR (400 MHz, MeOD) δ 7.66 – 7.30 (m, 9H, H_{Ar} BiPh), 4.45 (s, 2H, H_2-6'), 3.97 (dd, *J* = 11.7, 2.7 Hz, 1H, H-6a), 3.94 (dd, *J* = 11.7, 2.9 Hz, 1H, H-6b), 3.91 (dd, *J* = 3.7, 2.0 Hz, 1H, H-2), 3.75 (t, *J* = 9.1 Hz, 1H, H-4), 3.48 (t, *J* = 6.4 Hz, 2H, H_2-5'), 3.38 (d, *J* = 3.4 Hz, 1H, H-3), 3.05 (dd, *J* = 12.3, 3.9 Hz, 1H, H-1a), 2.84 (dt, *J* = 13.4, 8.5 Hz, 1H, H-1'a), 2.68 (dt, *J* = 13.4, 8.2 Hz, 1H, H-1'b), 2.57 (dd, *J* = 12.3, 1.8 Hz, 1H, H-1b), 2.22 (dt, *J* = 9.3, 2.7 Hz, 1H, H-5), 1.67 – 1.63 (m, 2H, H_2-4'), 1.57 – 1.54 (m, 2H, H_2-2'), 1.45 – 1.34 (m, 2H, H_2-3'). ^{13}C NMR (100 MHz, MeOD) δ 144.4 – 129.1 (C_{Ar} BiPh), 77.4 (C-3), 72.7 (C-6'), 72.3 (C-5'), 70.4 (C-2), 70.4 (C-4), 67.8 (C-5), 59.9 (C-6), 57.3 (C-1), 54.6 (C-1'), 31.4 (C-4'), 26.1 (C-3'), 25.9 (C-2'). $[\alpha]^{20}_D$ = +17.4 (c = 0.5, MeOH). IR/cm^{-1}: 3321, 2941, 2866, 2349, 2326, 1636, 1558, 1506, 1456, 1202, 1088, 744. HRMS: found 416.24303 $[C_{24}H_{33}NO_5+H]^+$, calculated for $[C_{24}H_{33}NO_5+H]^+$ 416.24315.

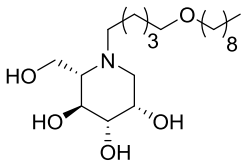
_N_-Benzyloxyethyl- L-_manno_-1-deoxynojimycin (135):



129 was subjected to the general procedure A and generated **135** (30 mg, 0.10 mmol) in a yield of 17%. ^{1}H NMR (400 MHz, MeOD) δ 7.58 – 7.28 (m, 5H, H_{Ar} Bn), 4.68 – 4.60 (m, 1H, H-2'a), 4.62 (s, 2H, CH_2 Bn),

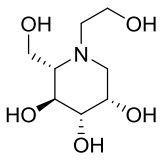
4.09 (dd, *J* = 12.7, 2.9 Hz, 1H, H-6a), 4.03 (dd, *J* = 12.7, 3.0 Hz, 1H, H-6b), 4.01 – 3.97 (m, 1H, H-2'b), 4.12 (dd, *J* = 3.8, 1.4 Hz, 1H, H-2), 3.94 (t, *J* = 9.2, 1H, H-4), 3.69 – 3.61 (m, 1H, 1H, H-1'a), 3.60 (dd, *J* = 9.1, 3.0 Hz, 1H, H-3), 3.34 – 3.29 (m, 1H, H-1'b), 3.18 (dd, *J* = 12.9, 4.0 Hz, H-1a), 3.09 (d, *J* = 9.6 Hz, 1H, H-5), 2.93 (d, *J* = 12.7 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, MeOD) δ 137.5 – 127.7 (C_{Ar} Bn), 72.9 (CH_2 Bn), 72.2 (C-3), 66.6 (C-5), 66.2 (C-4), 66.1 (C-2), 56.0 (C-2'), 55.0 (C-6), 53.2 (C-1), 52.1 (C-1'). $[\alpha]^{20}_D$ = +8.8 (c = 1.0, MeOH). IR/cm^{-1}: 3381, 2913, 1653, 1212, 1101, 1079, 1027. HRMS: found 298.16505 $[C_{15}H_{23}NO_5+H]^+$, calculated for $[C_{15}H_{23}NO_5+H]^+$ 298.16490.

N-[5-(Nonyloxy)pentyl]- L-*manno*-1-deoxynojimycin (136):



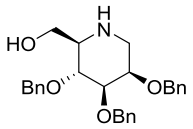
129 was subjected to the general procedure A and generated **136** (22 mg, 0.06 mmol) in a yield 29%. ^{1}H NMR (400 MHz, MeOD) δ 4.16 (s, 1H, H-2), 4.11 (dd, *J* = 12.8, 2.8 Hz, 1H, H-6a), 3.99 (dd, *J* = 12.6, 2.7 Hz, 1H, H-6b), 3.97 (t, *J* = 9.5 Hz, 1H, H-4), 3.61 (dd, *J* = 9.3, 3.0 Hz, 1H, H-3), 3.51 – 3.36 (m, 2H, H_2-1), 3.35 – 3.31 (m, 2H, H_2-1'), 3.48 (t, *J* = 6.4 Hz, 2H, H_2-5'), 3.46 (t, *J* = 6.6 Hz, 2H, H_2-6'), 3.13 – 3.06 (m, 1H, H-5), 1.89 – 1.73 (m, 2H, H_2-2'), 1.70 – 1.66 (m, 2H, H_2-4'), 1.61 – 1.58 (m, 2H, H_2-7'), 1.52 – 1.48 (m, 2H, H_2-3'), 1.43 – 1.27 (m, 12H, H_2-8' – H_2-13'), 0.93 (t, *J* = 7.0 Hz, 3H, H_3-14'). ^{13}C NMR (100 MHz, MeOD) δ 75.0 (C-3), 72.9 (C-6'), 72.2 (C-5'), 68.6 (C-5), 68.0 (C-2), 67.8 (C-4), 56.9 (C-1), 56.9 (C-6), 55.3 (C-1'), 33.9, 31.6, 31.6, 31.5, 31.3, 31.0, 28.1, 25.3, 24.6 (C-2' – C-4', C-7' – C-13'), 15.3 (C-14'). $[\alpha]^{20}_D$ = +9.8 (c = 1.0, MeOH). IR/cm^{-1}: 3200, 2870, 2509, 1456, 1398, 1317, 1246, 1101. HRMS: found 376.30575 $[C_{20}H_{41}NO_5+H]^+$, calculated for $[C_{20}H_{41}NO_5+H]^+$ 376.30575.

N-Hydroxyethyl- L-*manno*-1-deoxynojimycin (137)



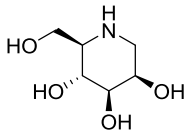
137 (4 mg, 0.02 mmol) was synthesized as described for the preparation of compound for **90a** in a yield of 40%. ^{1}H NMR (400 MHz, MeOD) δ 3.93 (td, *J* = 3.8, 1.8 Hz, 1H, H-2), 3.89 (dd, *J* = 11.1, 4.5 Hz, 1H, H-6a), 3.82 (dd, *J* = 11.1, 3.1 Hz, 1H, H-6b), 3.79 (dd, *J* = 11.5, 4.5 Hz, 1H, H-2'a), 3.72 (t, *J* = 9.8 Hz, 1H, H-4) 3.69 (dd, *J* = 11.7, 4.8 Hz, 1H, H-2'b), 3.50 (dd, *J* = 9.3, 3.2 Hz, 1H, H-3), 3.15 (dd, *J* = 12.6, 4.0 Hz, 1H, H-1a), 3.10 (dd, *J* = 13.9, 2.8 Hz, 1H, H-1'a), 2.85 (dd, *J* = 13.9, 1.6 Hz, 1H, H-1'b), 2.63 – 2.56 (m, 1H, H-1b), 2.49 (ddd, *J* = 9.9, 4.5, 3.1 Hz, 1H, H-5). ^{13}C NMR (100 MHz, MeOD) δ 77.5 (C-3), 70.7 (C-2), 70.3 (C-4), 63.6 (C-5), 62.8 (C-6), 60.8 (C-2'), 56.3 (C-1), 51.2 (C-1'). HRMS: found 208.11791 $[C_8H_{17}NO_5+H]^+$, calculated for $[C_8H_{17}NO_5+H]^+$ 208.11795

2,3,4-Tri-*O*-benzyl- D-*manno*-1-deoxynojimycin (138a):



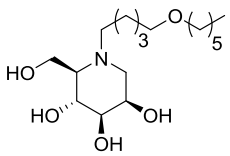
2,3,4-Tri-*O*-benzyl-5-*tert*-butyldimethylsilyl-*O*-D-*manno*-1-deoxynojimycin (0.84 g, 1.25 mmol) was dissolved in THF (8 mL) at r.t.. TBAF (1M in THF, 3.6 mL) was added to the solution under argon protection. The reaction mixture was stirred overnight, diluted with DCM, washed with water and brine, dried (Na_2SO_4) filtered and concentrated. The residual syrup was purified with silica gel column chromatography (20:1, DCM:MeOH) to give the protected **138a** (0.39 g, 0.9 mmol) with 72% yield. R_F = 0.45 (10:1, DCM:MeOH). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.47 – 7.27 (m, 15H, H_{Ar} Bn), 4.95 (d, *J* = 11.0 Hz, 1H, CH*H* Bn), 4.70 (d, *J* = 3.6 Hz, 2H, CH_2 Bn), 4.66 – 4.58 (m, 3H, 3 x CH*H* Bn), 3.82 (dd, *J* = 11.0, 3.4 Hz, 1H, H-6a), 3.80 (dd, *J* = 3.1, 1.3 Hz, 1H, H-2), 3.74 (t, *J* = 9.4 Hz, 1H, H-4), 3.62 (dd, *J* = 11.0, 5.9 Hz, 1H, H-6b), 3.53 (dd, *J* = 9.1, 2.9 Hz, 1H, H-3), 3.16 (dd, *J* = 14.2, 3.1 Hz, 1H, H-1a), 2.59 (ddd, *J* = 9.4, 5.8, 3.4 Hz, 1H, H-5), 2.51 (dd, *J* = 14.3, 1.4 Hz, 1H, H-1b), 2.41 (s, 1H, -OH). ^{13}C NMR (150 MHz, $CDCl_3$) δ 139.5 – 128.6 (C_{Ar} Bn), 85.0 (C-3), 78.0 (C-4), 76.2 (CH_2 Bn), 74.6 (C-2), 72.9 (CH_2 Bn), 72.6 (CH_2 Bn), 63.5 (C-6), 62.4 (C-5), 47.7 (C-1).

D-*Manno*-1-deoxynojimycin (138):



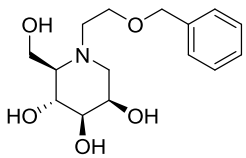
138a (0.39 g, 0.9 mmol) was dissolved in ethanol (50 mL), and pH of the solution was adjusted to 2 with aqueous HCl (1M). After the solvent flushed with argon (3 x), a catalyst amount of Pd/C (10%) was added. The reaction mixture was exposed to H_2 atmosphere (2 bar) for 18 hours. After TLC analysis showed completely consumption **138a**, 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 give **138** in a yield of 60% (0.09 g, 0.54 mmol). ^{1}H NMR (400 MHz, MeOD) δ 4.16 (td, *J* = 3.1, 1.6 Hz, 1H, H-2), 4.02 (dd, *J* = 11.8, 3.3 Hz, 1H, H-6a), 3.84 (dd, *J* = 10.3, 9.3 Hz, 1H, H-4), 3.83 (dd, *J* = 11.9, 7.0 Hz, 1H, H-1b), 3.61 (dd, *J* = 9.2, 3.0 Hz, 1H, H-3), 3.35 (dd, *J* = 13.5, 3.2 Hz, 1H, H-1a), 3.24 (dd, *J* = 13.2, 1.6 Hz, 1H, H-1b), 3.08 (ddd, *J* = 10.3, 7.0, 3.3 Hz, 1H, H-5). ^{13}C NMR (100 MHz, MeOD) δ 75.3 (C-3), 68.4 (C-4), 68.4 (C-2), 63.3 (C-5), 60.5 (C-6), 49.8 (C-1).

N-[5-(Hexyloxy)pentyl]-D-*manno*-1-deoxynojimycin (142):



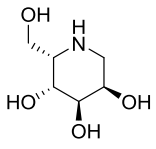
138 was subjected to the general procedure A and generated **142** (6.4 mg, 0.02 mmol) in a yield of 7%. ^{1}H NMR (400 MHz, MeOD) δ 4.05 – 4.03 (m, 1H, H-2), 4.03 (dd, *J* = 12.2, 3.1 Hz, 1H, H-6a), 3.95 (dd, *J* = 12.3, 2.9 Hz, 1H, H-6b), 3.86 (t, *J* = 9.2 Hz, 1H, H-4), 3.55 – 3.49 (m, 1H, H-3), 3.48 (t, *J* = 6.4 Hz, 2H, H_2-5'), 3.46 (t, *J* = 6.6 Hz, 2H, H_2-6'), 3.33 – 3.27 (m, 2H, H_2-1'), 3.18 – 2.99 (m, 2H, H_2-1), 1.78 – 1.27 (m, 14H, H_2-2', H_2-3', H_2-4', H_2-7', H_2-8', H_2-9', H_2-10'), 0.93 (t, *J* = 7.0 Hz, 3H, H_3-11'). ^{13}C NMR (100 MHz, MeOD) δ 75.8 (C-3), 72.9 (C-6'), 72.4 (C-5'), 68.3 (C-4), 68.3 (C-2), 58.0 (C-6), 56.6 (C-1'), 54.9 (C-1), 33.7, 31.6, 31.2, 27.8, 25.6, 25.2, 24.6 (C-2' – C-4', C-7' – C-10'), 15.2 (C-11'). IR/cm^{-1}: 3302, 2930, 2858, 2046, 1684, 1456, 1269, 1105. HRMS: found 334.25890 $[C_{17}H_{35}NO_5+H]^+$, calculated for $[C_{17}H_{35}NO_5+H]^+$ 334.25880.

N-Benzyloxyethyl-D-*manno*-1-deoxynojimycin (145):



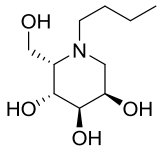
138 was subjected to the general procedure A and generated **145** (4.8 mg, 0.015 mmol) in a yield of 5%. ^{1}H NMR (400 MHz, MeOD) δ 7.48 – 7.31 (m, 5H, H_{Ar} Bn), 4.53 (s, 2H, CH_2 Bn) 4.33 (d, *J* = 13.2 Hz, 1H, H-2'a), 4.18 (dd, *J* = 11.8, 2.9 Hz, 1H). 4.03 (dd, *J* = 11.9, 2.8 Hz, 1H, H-6a), 3.97 (dd, *J* = 11.9, 2.7 Hz, 1H, H-6b), 3.90 (td, *J* = 3.7, 1.7 Hz, 1H, H-2), 3.75 (t, *J* = 9.1 Hz, 1H, H-4), 3.45 – 3.41 (m, 2H, H-2'b, H-3), 3.15 (dd, *J* = 12.5, 3.8 Hz, 1H, H-1a), 3.23 – 3.14 (m, 1H, H-1'a), 2.97 – 2.90 (m, 1H, H-1'b), 2.72 (dd, *J* = 12.4, 1.6 Hz, 1H, H-1b), 2.37 (dt, *J* = 9.0, 2.7 Hz, 1H, H-5). ^{13}C NMR (100 MHz, MeOD) δ 140.4 – 129.6 (C_{Ar} Bn), 77.3 (C-3), 75.1 (CH_2 Bn), 70.3 (C-2), 70.2 (C-4), 68.3 (C-5), 60.3 (C-6), 59.1 (C-2'), 57.9 (C-1), 53.7 (C-1'). IR/cm^{-1}: 3360, 2504, 1636, 1558, 1506, 1456, 1435, 1271, 1207, 1082, 1051. HRMS: found 298.16504 $[C_{15}H_{23}NO_5+H]^+$, calculated for $[C_{15}H_{23}NO_5+H]^+$ 298.16490.

L-*Gulo*-1-deoxynojimycin (146):



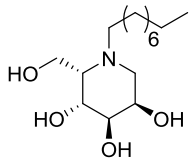
146 (0.15 g, 0.90 mmol) was synthesized as described for the preparation of compound **138** in a yield of 59%**.** ^{1}H NMR (400 MHz, MeOD) δ 4.22 (ddd, *J* = 11.5, 5.1, 2.7 Hz, 1H, H-2), 4.02 (dd, *J* = 4.6, 1.6 Hz, 1H, H-4), 3.99 (dd, *J* = 4.5, 2.8 Hz, 1H, H-3), 3.85 (dd, *J* = 11.8, 5.5 Hz, 1H, H-6a), 3.81 (dd, *J* = 11.8, 8.2 Hz, 1H, H-6b), 3.47 (ddd, *J* = 7.6, 5.5, 1.6 Hz, 1H, H-5), 3.18 (dd, *J* = 11.8, 5.1 Hz, 1H, H-1a), 3.08 (t, *J* = 11.7 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, MeOD) δ 69.0 (C-3), 67.4 (C-4), 62.6 (C-2), 59.2 (C-6), 55.6 (C-5), 42.7 (C-1). $[\alpha]^{20}_D$ = -24.8 (c = 1.0, MeOH). IR/cm^{-1}: 3350, 3034, 1634, 1436, 1126, 1078, 1051, 1015. HRMS: found 164.09164 $[C_6H_{13}NO_4+H]^+$, calculated for $[C_6H_{13}NO_4+H]^+$ 164.09173.

N-Butyl-L-*gulo*-1-deoxynojimycin (147):



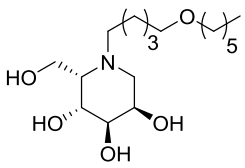
146 was subjected to the general procedure A and generated **147** (7 mg, 0.03 mmol) in a yield of 35%. ^{1}H NMR (600 MHz, MeOD) δ 4.16 – 4.12 (m, 1H, H-2), 4.06 (dd, *J* = 4.9, 2.4 Hz, 1H, H-4), 3.97 (dd, *J* = 11.9, 5.0 Hz, 1H, H-6a), 3.94 (d, *J* = 5.0 Hz, 1H, H-6b), 3.89 (dd, *J* = 4.7, 3.1 Hz, 1H, H-3), 3.15 – 2.81 (m, 5H, H-5, H_2-1', H_2-1), 1.76 – 1.60 (m, 2H, H_2-2'), 1.46 – 1.42 (m, 2H, H_2-3'), 1.06 (t, *J* = 7.4 Hz, 3H, H_3-4'). ^{13}C NMR (150 MHz, MeOD) δ 73.5 (C-4), 72.4 (C-3), 66.9 (C-2), 62.1 (C-6), 62.0 (C-5), 55.5 (C-1'), 53.3 (C-1), 26.3 (C-2'), 22.4 (C-3'), 15.1 (C-4'). $[\alpha]^{20}_D$ = +55.0 (c = 0.1, MeOH). IR/cm^{-1}: 3335, 2974, 2928, 2900, 2349, 1636, 1456, 1379, 1271, 1083, 1043. HRMS: found 220.15440 $[C_{10}H_{21}NO_4+H]^+$, calculated for $[C_{10}H_{21}NO_4+H]^+$ 220.15433.

N-Nonyl-L-*gulo*-1-deoxynojimycin (148):



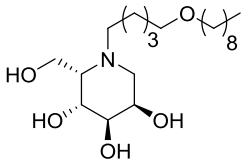
146 was subjected to the general procedure A and generated **148** (8 mg, 0.03 mmol) in a yield of 31%. ^{1}H NMR (400 MHz, MeOD) δ 4.22 (ddd, *J* = 9.0, 6.3, 2.9 Hz, 1H, H-2), 4.11 (dd, *J* = 4.7, 2.1 Hz, 1H, H-4), 4.01 (dd, *J* = 12.0, 4.7 Hz, 1H, H-6a), 3.97 (dd, *J* =12.0, 5.0 Hz, 1H, H-6b), 3.93 (dd, *J* = 4.6, 2.9 Hz, 1H, H-3), 3.34 (td, *J* = 4.8, 2.2 Hz, 1H, H-5), 3.18 (ddd, *J* = 9.5, 6.7, 2.3 Hz, 2H, H_2-1'), 3.15 – 3.10 (m, 2H, H_2-1), 1.93 – 1.69 (m, 2H, H_2-2'), 1.54 – 1.33 (m, 12H, H_2-3' – H_2-8'), 0.93 (t, *J* = 7.0 Hz, 3H, H_3-9'). ^{13}C NMR (100 MHz, MeOD) δ 72.6 (C-4), 71.2 (C-3), 65.3 (C-2), 62.0 (C-5), 61.3 (C-6), 55.0 (C-1'), 52.0 (C-1), 33.4, 30.8, 30.8, 28.3, 28.3, 24.3 (C-2' – C-8'), 14.9 (C-9'). $[\alpha]^{20}_D$ = +14.4 (c = 0.5, MeOH). IR/cm^{-1}: 3336, 2925, 2854, 1653, 1468, 1378, 1145, 1064, 979, 667. HRMS: found 290.23272 $[C_{15}H_{31}NO_4+H]^+$, calculated for $[C_{15}H_{31}NO_4+H]^+$ 290.23258.

N-[5-(Hexyloxy)pentyl]-L-*gulo*-1-deoxynojimycin (149):



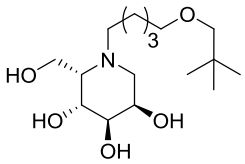
146 was subjected to the general procedure A and generated **149** (9 mg, 0.03 mmol) in a yield of 30%. ^{1}H NMR (400 MHz, MeOD) δ 4.14 (ddd, *J* = 10.2, 4.5, 3.0 Hz, 1H, H-2), 4.06 (dd, *J* = 4.8, 2.3 Hz, 1H, H-4), 3.98 (dd, *J* = 11.7, 4.7 Hz, 1H, H-6a), 3.94 (d, *J* = 12.0, 4.5 Hz, 1H), 3.89 (dd, *J* = 4.7, 3.1 Hz, 1H, H-3), 3.53 (t, *J* = 6.5 Hz, 2H, H_2-5'), 3.51 (t, *J* = 6.6 Hz, 2H, H_2-6') , 3.23 – 2.85 (m, 5H, H-5, H_2-1', H_2-1), 1.90 – 1.31 (m, 14H, H_2-2', H_2-3', H_2-4', H_2-7', H_2-8', H_2-9', H_2-10'), 0.94 (t, *J* = 7.0 Hz, 3H, H_3-11'). ^{13}C NMR (100 MHz, MeOD) δ 73.0 (C-4), 72.8 (C-6'), 72.4 (C-5'), 72.1 (C-3), 66.8 (C-2), 62.0 (C-6), 62.0 (C-5), 55.5 (C-1'), 53.1 (C-1), 33.4, 31.2, 31.1, 27.6, 25.4, 25.2, 24.3 (C-2' – C-4', C-7' – C-10'), 15.0 (C-11'). $[\alpha]^{20}_D$ = +27.0 (c = 0.1, MeOH). IR/cm^{-1}: 3380, 2987, 2872, 2376, 1635, 1506, 1456, 1394, 1229, 1076. HRMS: found 334.25886 $[C_{17}H_{35}NO_5+H]^+$, calculated for $[C_{17}H_{35}NO_5+H]^+$ 334.25880.

N-[5-(Nonyloxy)pentyl]-L-*gulo*-1-deoxynojimycin (150):



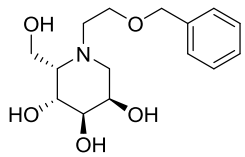
146 was subjected to the general procedure A and generated **150** (8 mg, 0.02 mmol) in a yield of 24%. ^{1}H NMR (400 MHz, MeOD) δ 4.28 (ddd, *J* = 11.1, 5.2, 2.8 Hz, 1H, H-2), 4.17 (dd, *J* = 4.4, 1.7 Hz, 1H, H-4), 4.06 (dd, *J* = 12.9, 4.1 Hz, 1H, H-6a), 4.01 (dd, *J* = 12.9, 4.8 Hz, 1H, H-6b), 3.97 (dd, *J* = 4.1, 3.0 Hz, 1H, H-3), 3.58 – 3.55 (m, 1H, H-5), 3.55 (t, *J* = 5.5 Hz, 2H, H_2-5'), 3.52 (t, *J* = 6.3 Hz, 2H, H_2-6'), 3.39 – 3.30 (m, 2H, H_2-1'), 3.31 – 3.20 (m, 2H, H_2-1), 3.71 – 3.64 (m, 2H, H_2-2'), 2.01 – 1.81 (m, 2H, H_2-7'), 1.77 – 1.70 (m, 2H, H_2-4'), 1.71 – 1.62 (m, 2H, H_2-3'), 1.63 – 1.48 (m, 12H, H_2-8', H_2-9', H_2-10', H_2-11', H_2-12', H_2-13'), 0.94 (t, *J* = 7.0 Hz, 3H, H_3-14'). ^{13}C NMR (100 MHz, MeOD) δ 73.2 (C-4), 72.9 (C-6'), 72.3 (C-5'), 70.9 (C-3), 65.0 (C-2), 62.6 (C-5), 62.0 (C-6), 55.8 (C-1'), 52.1 (C-1), 33.9, 31.9, 31.6, 31.6, 31.5, 31.3, 31.0, 28.1, 25.4, 23.9 (C-2' –C-4', C-7' – C-13'), 15.2 (C-14'). IR/cm^{-1}: 3308, 2927, 2872, 2313, 1636, 1456, 1394, 1204, 1057. $[\alpha]^{20}_D$ = +6.5 (c = 0.2, MeOH). HRMS: found 376.30576 $[C_{20}H_{41}NO_5+H]^+$, calculated for $[C_{20}H_{41}NO_5+H]^+$ 376.30575.

N-[5-(3,3-Dimethyl-1-propyloxy)pentyl]-L-*gulo*-1-deoxynojimycin (151):



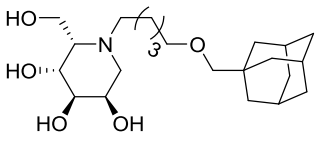
146 was subjected to the general procedure A and generated **151** (8 mg, 0.03 mmol) in a yield of 28%. ^{1}H NMR (600 MHz, MeOD) δ 4.09 (dd, *J* = 9.0, 4.8 Hz, 1H, H-2), 4.03 (td, *J* = 4.4, 2.1 Hz, 1H, H-4), 3.94 (dd, *J* = 11.7, 5.2 Hz, 1H, H-6a), 3.90 (dd, *J* = 11.6, 4.8 Hz, 1H, H-6b), 3.86 (dd, *J* = 4.8, 3.2 Hz, 1H, H-3), 3.51 (t, *J* = 6.4 Hz, 2H, H_2-5'), 3.16 (s, 2H, H_2-6'), 2.99 – 2.75 (m, 5H, H-5, H_2-1', H_2-1), 1.79 – 1.62 (m, 4H, H_2-4', H_2-2'), 1.50 – 1.41 (m, 2H, H_2-3'), 0.99 (s, 9H, H_3-8', H_3-9', H_3-10'). ^{13}C NMR (150 MHz, MeOD) δ 83.4 (C-6'), 73.6 (C-4), 73.2 (C-5'), 72.7 (C-3), 67.9 (C-2), 62.4 (C-6), 61.8 (C-5), 55.7 (C-1'), 53.6 (C-1), 33.8 (C-7'), 31.4 (C-4'), 28.0 (C-8', C-9', C-10'), 26.1 (C-2'), 25.4 (C-3'). $[\alpha]^{20}_{D}$ = +29.0 (c = 0.1, MeOH). IR/cm^{-1}: 3422, 2953, 2900, 2866, 2374, 2349, 2312, 1683, 1506, 1394, 1373, 1317, 1074. HRMS: found 320.24327 $[C_{16}H_{33}NO_5+H]^+$, calculated for $[C_{16}H_{33}NO_5+H]^+$ 320.24315.

N-Benzyloxyethyl-L-*gulo*-1-deoxynojimycin (152a):



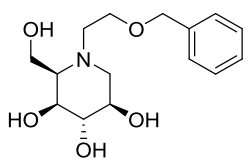
146 was subjected to the general procedure A and generated **152a** (13 mg, 0.04 mmol) in a yield of 22%. ^{1}H NMR (400 MHz, MeOD) δ 7.52 – 7.29 (m, 5H, H_{Ar} Bn), 4.63 (s, 2H, CH_2 Bn), 4.01 – 3.99 (m, 1H, H-2), 3.95 (dd, *J* = 11.7, 4.9 Hz, 1H, H-6a), 3.90 (dd, *J* = 11.7, 5.4 Hz, 1H, H-6b), 3.84 (td, *J* = 5.0, 2.6 Hz, 1H, H-3), 3.76 (dd, *J* = 5.2, 3.5 Hz, 1H, H-4), 3.59 (d, *J* = 13.5 Hz, 1H, H-2'a), 3.24 – 3.12 (m, 1H, H-1'a), 3.07 – 3.00 (m, 2H, H-1'b, H-2'b), 2.91 (t, *J* = 5.3 Hz, 1H, H-5), 2.76 (dd, *J* = 11.4, 4.3 Hz, 1H, H-1a), 2.46 (dd, *J* = 11.1, 9.6 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, MeOD) δ 131.9 – 129.6 (CH_{Ar} Bn), 75.1 (CH_2 Bn), 73.5 (C-3), 69.0 (C-4), 68.4 (C-2), 63.1 (C-5), 62.2 (C-6), 60.0 (C-2'), 54.4 (C-1'), 53.4 (C-1). $[\alpha]^{20}_{D}$ = +35.2 (c = 0.5, MeOH). IR/cm^{-1}: 3345, 2924, 1653, 1506, 1457, 1201, 1074, 1037. HRMS: found 298.16500 $[C_{15}H_{23}NO_5+H]^+$, calculated for $[C_{15}H_{23}NO_5+H]^+$ 298.16490.

N-[5-(Adamantan-1-yl-methoxy)pentyl]-L-*gulo*-1-deoxynojimycin (79):



146 was subjected to the general procedure A and generated **79** (7 mg, 0.02 mmol) in a yield of 19%. ^{1}H NMR (400 MHz, MeOD) δ 4.16 (ddd, *J* = 10.1, 4.8, 3.0 Hz, 1H, H-2), 4.07 (dd, *J* = 4.7, 2.3 Hz, 1H, H-4), 3.90 (dd, *J* = 4.7, 3.1 Hz, 1H, H-3), 3.99 (dd, *J* = 12.0, 4.9 Hz, 1H,), 3.94 (dd, *J* = 12.0, 4.8 Hz, 1H), 3.59 (t, *J* = 7.3 Hz, 2H, H_2-5'), 3.54 (t, *J* = 6.2 Hz, 2H, H_2-6'), 3.14 (td, *J* = 4.7, 2.0 Hz, 1H, H-5), 3.11 – 3.02 (m, 2H, H_2-1'), 3.00 (dd, *J* = 11.2, 4.9 Hz, 1H, H-1a), 2.93 (t, *J* = 10.7 Hz, 1H, H-1b), 2.04 – 2.02 (m, 3H, 3 x CH ada), 1.89 – 1.72 (m, 8H, 3 x CH_2 ada, H_2-2'), 1.72 – 1.61 (m, 8H, 3 x CH_2 ada, H_2-3'), 1.46 (td, *J* = 7.3, 3.4 Hz, 2H, H-4'). ^{13}C NMR (100 MHz, MeOD) δ 73.4 (C-4), 72.2 (C-3), 72.2 (C-6'), 68.7 (C-5'), 66.5 (C-2), 62.0 (C-5), 61.6 (C-6), 55.4 (C-1'), 53.1 (C-1), 45.6 (C-4'), 44.7 (CH_2 ada), 39.1 (CH_2 ada), 33.7 (C_q ada), 31.0 (CH ada), 29.2 (C-3'), 20.5 (C-2'). $[\alpha]^{20}_{D}$ = +18.0 (c = 0.1, MeOH). IR/cm^{-1}: 3300, 2978, 2901, 2349, 1635, 1489, 1259, 1082, 1045, 878. HRMS: found 398.29004 $[C_{22}H_{39}NO_5+H]^+$, calculated for $[C_{22}H_{39}NO_5+H]^+$ 398.29010.

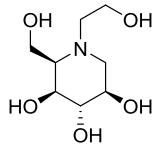
N-Benzyloxyethyl-D-*ido*-1-deoxynojimycin (157):



D-*ido*-DNJ was subjected to the general procedure A and generated **157** (44.8 mg, 0.15 mmol) in a yield of 25%. ^{1}H NMR (400 MHz, MeOD) δ 7.47 – 7.30 (m, 5H, H_{Ar} Bn), 4.62 (s, 2H, CH_2 Bn), 4.00 (dd, *J* = 11.6, 9.6 Hz, 1H, H-6a), 3.92 (dd, *J* = 11.6, 8.8 Hz, 1H, H-6b), 3.81 (dd, *J* = 8.9, 5.3 Hz, 1H, H-4), 3.69 (t, *J* = 5.7 Hz, 2H, H_2-2'), 3.67 – 3.61 (m, 1H, H-2), 3.45 (t, *J* = 8.5 Hz, 1H, H-3), 3.17 (q, *J* = 5.5 Hz, 1H, H-5), 3.11 (t, *J* = 5.6 Hz, 1H, H-1'a), 3.03 (t, *J* = 5.6 Hz, 1H, H-1'b), 2.97 (dd, *J* = 13.0, 5.1 Hz, 1H, H-1a), 2.74 (dd, *J* = 11.9, 9.1 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, MeOD) δ 140.4 – 128.9 (C_{Ar} Bn), 76.7 (C-3), 75.0 (CH_2 Bn), 73.3 (C-4), 71.9 (C-2), 70.7 (C-2'), 65.9 (C-5), 58.8 (C-6), 56.1 (C-1'), 53.7 (C-1). IR/cm^{-1}: 3330,

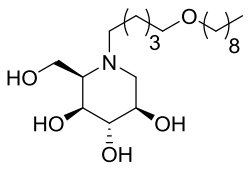
2950, 1653, 1456, 1362, 1272, 1209, 1058, 1027, 735. $[\alpha]^{20}_D$ = +18.0 (c = 1.0, MeOH). HRMS: found 298.16501 $[C_{15}H_{23}NO_5+H]^+$, calculated for $[C_{15}H_{23}NO_5+H]^+$ 298.16490.

N-Hydroxyethyl-D-*ido*-1-deoxynojimycin (158):



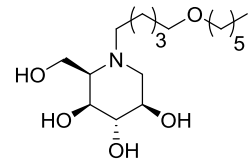
158 (12.1 mg, 0.06 mmol) was synthesized as described for the preparation of compound **90a** in a yield of 30%. ^{1}H NMR (400 MHz, MeOD) δ 4.15 (br s, 1H, H-3), 4.13 – 3.95 (m, 5H, H_2-6 H-2'a, H-2, H-4), 3.91 (dd, *J* = 11.9, 5.1 Hz, 1H, H-2'b), 3.78 (t, *J* = 5.0 Hz, 1H, H-5), 3.72 (d, *J* = 13.5 Hz, 1H, H-1a), 3.58 – 3.49 (m, 1H, H-1b), 3.46 (d, *J* = 13.3 Hz, 1H, H-1'a), 3.34 (dd, *J* = 13.4, 2.4 Hz, 1H, H-1'b). ^{13}C NMR (100 MHz, MeOD) δ 72.8 (C-3), 69.9 (C-4), 68.7 (C-2), 65.5 (C-5), 61.4 (C-2'), 57.4 (C-6), 57.4 (C-1), 47.7 (C-1'). $[\alpha]^{20}_D$ = -6.0 (c = 0.2, MeOH). IR/cm^{-1}: 3421, 2987, 2901, 2374, 1684, 1558, 1506, 1456, 1317, 1074. HRMS: found 208.11790 $[C_8H_{17}NO_5+H]^+$, calculated for $[C_8H_{17}NO_5+H]^+$ 208.11795.

N-[5-(Nonyloxy)pentyl]-D-*ido*-1-deoxynojimycin (159):



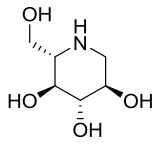
D-*ido*-DNJ (**153**) was subjected to the general procedure A and generated **159** (36.2 mg, 0.10 mmol) in a yield of 20%. ^{1}H NMR (400 MHz, MeOD) δ 3.94 (dd, *J* = 11.5, 4.8 Hz, 1H, H-6a), 3.90 (dd, *J* = 11.4, 6.4 Hz, 1H, H-6b), 3.78 (dd, *J* = 8.8, 5.2 Hz, 1H, H-4), 3.62 (ddd, *J* = 9.4, 8.0, 4.9 Hz, 1H, H-2), 3.52 (t, *J* = 6.5 Hz, 2H, H_2-5'), 3.51 (t, *J* = 6.6 Hz, 2H, H_2-6'), 3.46 (t, *J* = 8.4 Hz, 1H, H-3), 3.15 – 3.08 (m, 1H, H-5), 2.89 (dd, *J* = 12.4, 4.8 Hz, 1H, H-1a), 2.86 – 2.83 (m, 1H, H-1'a), 2.79 – 2.70 (m, 1H, H-1'b), 2.67 (dd, *J* = 12.4, 9.5 Hz, 1H, H-1b), 1.75 – 1.54 (m, 6H, H_2-2', H_2-4', H_2-7'), 1.53 – 1.26 (m, 14H, H_2-3', H_2-8', H_2-9', H_2-10', H_2-11', H_2-12', H_2-13'), 0.93 (t, *J* = 7.0 Hz, 3H, H_3-14'). ^{13}C NMR (100 MHz, MeOD) δ 76.7 (C-3), 73.6 (C-4), 72.8 (C-6'), 72.7 (C-5'), 72.1 (C-2), 65.2 (C-5), 58.5 (C-6), 56.4 (C-1'), 53.7 (C-1), 33.9, 31.6, 31.6, 31.5, 31.3, 29.3, 28.1, 25.8, 24.6 (C-2' – C-4', C-7' – C-13'), 15.3 (C-14'). $[\alpha]^{20}_D$ = +24.9 (c = 1.0, MeOH). HRMS: found 376.30605 $[C_{20}H_{41}NO_5+H]^+$, calculated for $[C_{20}H_{41}NO_5+H]^+$ 376.30575.

N-[5-(Hexyloxy)pentyl]-D-*ido*-1-deoxynojimycin (160):



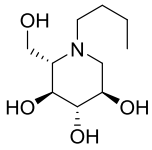
D-*ido*-DNJ (**153**) was subjected to the general procedure A and generated **160** (40.8 mg, 0.12 mmol) in a yield of 20%. ^{1}H NMR (400 MHz, MeOD) δ 4.20 – 3.86 (m, 5H, H-2, H_2-6, H-4, H-3), 3.64 (br s, 1H, H-5), 3.57 – 3.53 (m, 1H, H-1a), 3.55 (t, *J* = 6.3 Hz, 1H, H-5'), 3.52 (t, *J* = 6.6 Hz, 2H, H_2-6'), 3.49 – 3.40 (m, 3H, H_2-1', H-1b), 2.07 – 1.78 (m, 2H, H_2-2'), 1.78 – 1.69 (m, 2H, H_2-4'), 1.66 – 1.64 (m, 2H, H_2-7'), 1.60 – 1.51 (m, 2H, H_2-3'), 1.50 – 1.28 (m, 6H, H_2-8', H_2-9', H_2-10'), 0.93 (t, *J* = 7.0 Hz, 3H, H_3-11'). ^{13}C NMR (100 MHz, MeOD) δ 73.0 (C-2), 72.9 (C-6'), 72.3 (C-5'), 69.7 (C-4), 68.9 (C-3), 64.7 (C-5), 62.2 (C-6), 56.2 (C-1'), 55.9 (C-1), 33.7 , 31.6, 31.0, 27.8, 25.3, 25.3, 24.5 (C-2' – C-4', C-7' – C-10'), 15.3 (C-11'). $[\alpha]^{20}_D$ = -4.2 (c = 1.0, MeOH). IR/cm^{-1}: 3385, 2932, 2859, 1628, 1435, 1269, 1096, 1067. HRMS: found 334.25887 $[C_{17}H_{35}NO_5+H]^+$, calculated for $[C_{17}H_{35}NO_5+H]^+$ 334.25880.

L-*Gluco*-1-deoxynojimycin (161):



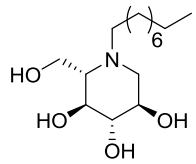
^{1}H NMR (400 MHz, MeOD) δ 3.93 (dd, *J* = 11.8, 3.3 Hz, 1H, H-6a), 3.85 (dd, *J* = 11.8, 5.5 Hz, 1H, H-6b), 3.69 (ddd, *J* = 11.4, 9.1, 5.1 Hz, 1H, H-2), 3.51 (dd, *J* = 10.4, 9.0 Hz, 1H, H-4), 3.38 (t, *J* = 9.1 Hz, 1H, H-3), 3.34 (dd, *J* = 12.4, 5.1 Hz, H-1a), 3.06 (ddd, *J* = 10.4, 5.5, 3.3 Hz, 1H, H-5), 2.87 (dd, *J* = 12.4, 11.4 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, MeOD) δ 77.1 (C-3), 68.3 (C-4), 67.5(C-2), 60.5 (C-5), 57.9 (C-6), 46.4 (C-1). $[\alpha]^{20}_D$ = -34.8 (c = 1.0, MeOH). IR/cm^{-1}: 3315, 2945, 2497, 1616, 1417, 1093, 1043, 1022. HRMS: found 164.09172 $[C_6H_{13}NO_4+H]^+$, calculated for $[C_6H_{13}NO_4+H]^+$ 164.09173.

N-Butyl-L-*gluco*-1-deoxynojimycin (162):



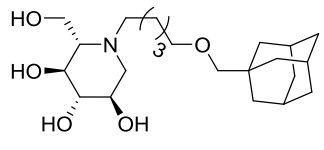
161 was subjected to the general procedure A and generated **162** (53.9 mg, 0.25 mmol) in a yield of 40%. ^{1}H NMR (400 MHz, MeOD) δ 4.12 (dd, *J* = 12.5, 1.9 Hz, 1H, H-6a), 3.94 (dd, *J* = 12.5, 3.1 Hz, 1H, H-6b), 3.73 (ddd, *J* = 11.2, 9.2, 4.9 Hz, 1H, H-2), 3.62 (dd, *J* = 10.3, 9.2 Hz, 1H, H-4), 3.47 (dd, *J* = 12.1, 4.9 Hz, 1H, H-1), 3.40 (t, *J* = 9.3 Hz, 1H, H-3), 3.33 (m, 1H, H-1'a), 3.22 (dt, *J* = 12.7, 6.5 Hz, 1H, H-1'b), 3.06 (d, *J* = 10.2 Hz, 1H, H-5), 2.99 (t, *J* = 11.7 Hz, 1H, H-1b), 1.78 – 17.4 (m, 2H, H_2-2'), 1.47 – 1.45 (m, 2H, H_2-3'), 1.04 (t, *J* = 7.4 Hz, 3H, H_3-4'). ^{13}C NMR (100 MHz, MeOD) δ 76.8 (C-3), 66.5 (C-4), 67.6 (C-2), 66.1 (C-5), 53.7 (C-6), 52.4 (C-1), 52.7 (C-1'), 24.9 (C-2'), 19.6 (C-3'), 12.6 (C-4'). IR/cm^{-1}: 3320, 3038, 2962, 2873, 1653, 1398, 1099, 1086, 1050, 1028, 936, 886. $[\alpha]^{20}_{D}$ = +1.2 (c = 1.0, MeOH). HRMS: found 220.15428 $[C_{10}H_{21}NO_4+H]^+$, calculated for $[C_{10}H_{21}NO_4+H]^+$ 220.15433.

N-Nonyl-L-*gluco*-1-deoxynojimycin (163):



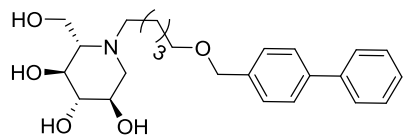
161 was subjected to the general procedure A and generated **163** (63.5 mmol, 0.22 mmol) in a yield of 37%. ^{1}H NMR (400 MHz, MeOD) δ 4.10 (d, *J* = 12.5 Hz, 1H, H-6a), 3.92 (dd, *J* = 12.4, 3.0 Hz, 1H, H-6b), 3.69 (td, *J* = 10.3, 4.7 Hz, 1H, H-2), 3.59 (t, *J* = 9.7 Hz, 1H, H-4), 3.42 (dd, *J* = 12.1, 4.7 Hz, 1H, H-1a), 3.37 (t, *J* = 9.2 Hz, 1H, H-3), 3.32 – 3.24 (m, 1H, H-1'a), 3.20 – 3.10 (m, 1H, H-1'b), 3.02 – 2.84 (m, 2H, H-5, H-1b), 1.88 – 1.61 (m, 2H, H_2-2'), 1.51 – 1.24 (m, 12H, H_2-3', H_2-4', H_2-5', H_2-6', H_2-7', H_2-8'), 0.93 (t, *J* = 7.0 Hz, 3H, H_3-9'). ^{13}C NMR (100 MHz, MeOD) 77.0 (C-3), 67.7 (C-4), 66.7 (C-2), 66.0 (C-5), 54.0 (C-6), 53.7 (C-1), 52.8 (C-1'), 31.6, 29.1, 28.9, 28.9, 26.4, 22.9, 22.3 (C-2'- C-8'), 13.0 (C-9'). $[\alpha]^{20}_{D}$ = +4.3 (c = 1.0, MeOH). IR/cm^{-1}: 3333, 2924, 2855, 1456, 1374, 1085, 1026, 952, 886, 721. HRMS: found 290.23260 $[C_{15}H_{31}NO_4+H]^+$, calculated for $[C_{15}H_{31}NO_4+H]^+$ 290.23258.

N-[5-(adamantan-1-yl-methoxy)pentyl]-L-*gluco*-1-deoxynojimycin (76):



161 was subjected to the general procedure A and generated **76** (11 mg, 0.03 mmol) in a yield of 14%. ^{1}H NMR (400 MHz, MeOD) δ 3.96 (d, *J* = 2.7 Hz, 2H, H_2-6), 3.58 (ddd, *J* = 10.6, 9.1, 4.9 Hz, 1H, H-2), 3.48 (t, *J* = 6.4 Hz, 2H, H_2-5'), 3.40 (t, *J* = 9.2 Hz, 1H, H-4), 3.24 (t, *J* = 9.1 Hz, 1H, H-3), 3.12 (dd, *J* = 11.3, 4.9 Hz, 1H, H-1a), 2.94 (ddd, *J* = 13.4, 9.6, 6.7 Hz, 1H, H-1'a), 2.74 (ddd, *J* = 13.3, 9.4, 6.1 Hz, 1H, H-1'b), 2.35 (t, *J* = 11.0 Hz, 1H, H-1b), 2.30 (dt, *J* = 9.6, 2.8 Hz, 1H, H-5), 2.05 – 2.03 (m, 3H, 3 x CH ada), 1.89 – 1.74 (m, 6H, 3 x CH_2 ada), 1.65 (d, *J* = 2.8 Hz, 6H, 3 x CH_2 ada), 1.72 – 1.59 (m, 4H, H_2-2', H_2-4'), 1.54 – 1.37 (m, 2H, H_2-3'). ^{13}C NMR (100 MHz, MeOD) δ 83.9 (C-6'), 81.2 (C-3), 73.3 (C-5'), 72.6 (C-4), 71.3 (C-2), 68.2 (C-5), 59.8 (C-6), 58.3 (C-1), 54.7 (C-1'), 41.7 (CH_2 ada), 39.2 (CH_2 ada), 36.0 (C_q ada), 31.4 (C-4'), 30.6 (CH ada), 26.1 (C-2'), 25.8 (C-3'). $[\alpha]^{20}_{D}$ = +6.4 (c = 0.5, MeOH). HRMS: found 398.28980 $[C_{22}H_{39}NO_5+H]^+$, calculated for $[C_{22}H_{39}NO_5+H]^+$ 398.29010

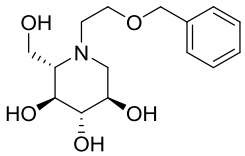
N-[(Biphenyl-4-yl-methoxy)pentyl]-L-*gluco*-1-deoxynojimycin (164):



161 was subjected to the general procedure A and generated **164** (28 mg, 0.07 mmol) in a yield of 22%. ^{1}H NMR (400 MHz, MeOD) δ 7.64 – 7.29 (m, 9H, H_{Ar} BiPh), 3.95 (dd, *J* = 12.0, 2.6 Hz, 1H, H-6a), 3.91 (dd, *J* = 12.0, 2.8 Hz, 1H, H-6b), 3.57 (ddd, *J* = 10.5, 9.1, 4.8 Hz, 1H, H-2), 3.48 – 3.43 (m, 2H, H_2-5'), 3.45 (t, *J* = 9.3 Hz, 1H, H-4), 3.23 (t, *J* = 9.1 Hz, 1H, H-3), 3.07 (dd, *J* = 11.2, 4.9 Hz, 1H, H-1a), 2.86 (dt, *J* = 13.4, 7.5 Hz, 1H, H-1'a), 2.65 (dt, *J* = 15.4, 6.9 Hz, 1H, H-1'b), 2.26 (t, *J* = 10.8 Hz, 1H, H-1b), 2.19 (dt, *J* = 9.5, 2.8 Hz, 1H, H-5), 1.64 (p, *J* = 7.0 Hz, 2H, H_2-4'), 1.56 (p, *J* = 7.8 Hz, 2H, H_2-2'), 1.41 – 1.37 (m, 2H, H_2-3'). ^{13}C NMR (100 MHz, MeOD) δ 144.4 – 129.1 (C_{Ar} BiPh), 81.4 (C-3), 72.8 (C-4), 72.6 (C-6'), 72.3 (C-5'), 71.6 (C-2), 68.1 (C-5), 60.3 (C-6), 58.5 (C-1), 54.5 (C-1'), 31.4 (C-4'), 26.1 (C-3'), 25.8 (C-2'). IR/cm^{-1}: 3322, 2933, 2861, 1646,

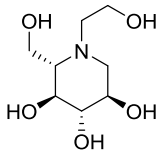
1479, 1456, 1362, 1268, 1198, 1156, 1085, 1034, 1009. $[\alpha]^{20}_D$ = -31.7 (c = 1, MeOH). HRMS: found 416.24299 $[C_{24}H_{33}NO_5+H]^+$, calculated for $[C_{24}H_{33}NO_5+H]^+$ 416.24315.

N-Benzyloxyethyl -L-*gluco*-1-deoxynojimycin (165):



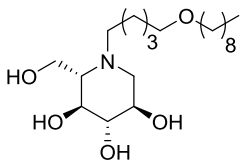
161 was subjected to the general procedure A and generated **165** (13 mg, 0.04 mmol) in a yield of 15%. ^{1}H NMR (400 MHz, MeOD) δ 7.51 – 7.26 (m, 5H, H_{Ar} Bn), 4.62 (s, 2H, CH_2 Bn), 3.99 (dd, *J* = 11.5, 9.9 Hz, 1H, H-6a), 3.91 (t, *J* = 11.4 Hz, 1H, H-6b), 3.81 (dd, *J* = 8.9, 5.3 Hz, 1H, H-4), 3.70 (t, *J* = 5.7 Hz, 2H, H_2-2'), 3.66 – 3.58 (m, 1H, H-2), 3.46 (t, *J* = 8.5 Hz, 1H, H-3), 3.18 (dd, *J* = 11.7, 5.3 Hz, 1H, H-5), 3.13 (dd, *J* = 13.8, 5.6 Hz, H-1'a), 3.03 (dd, *J* = 13.7, 5.6 Hz, H-1'b), 2.98 (dd, *J* = 12.7, 4.9 Hz, 1H, H-1a), (dd, *J* = 12.5, 9.7 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, MeOD) δ 140.4 – 129.6 (C_{Ar} Bn), 76.6 (C-3), 75.0 (CH_2 Bn), 73.3 (C-4), 71.9 (C-2), 70.4 (C-2'), 65.7 (C-5), 58.8 (C-6), 56.1 (C-1'), 52.7 (C-1). IR/cm^{-1}: 3328, 2878, 1670, 1456, 1362, 1261, 1203, 1136, 1059, 1027. $[\alpha]^{20}_D$ = -9.3 (c = 1.0, MeOH). HRMS: found 298.16502 $[C_{15}H_{23}NO_5+H]^+$, calculated for $[C_{15}H_{23}NO_5+H]^+$ 298.16490.

N-Hydroxyethyl-L-*gluco*-1-deoxynojimycin (166):



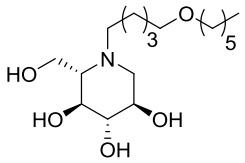
166 (14 mg, 0.07 mmol) was synthesized as described for the preparation of compound **90a** in a yield of 47%. ^{1}H NMR (400 MHz, MeOD) δ 4.17 – 4.11 (m, 1H, H-3), 4.11 – 3.98 (m, 3H, H_2-6, H-2'a), 4.07 (ddd, *J* = 10.4, 6.7, 3.6 Hz, 1H, H-2), 3.99 – 3.93 (m, 1H, H-4), 3.88 (dd, *J* = 11.7, 4.8 Hz, 1H, H-2'b), 3.75 – 3.66 (m, 1H, H-1a), 3.58 – 3.48 (m, 2H, H-5, H-1b), 3.45 (dd, *J* = 13.1, 2.1 Hz, 1H, H-1'a), 3.32 (dd, *J* = 13.4, 3.3 Hz, 1H, H-1'b). ^{13}C NMR (100 MHz, MeOD) δ 73.1 (C-3), 70.1 (C-4), 69.3 (C-2), 61.6 (C-2'), 59.2 (C-5), 57.5 (C-6), 57.4 (C-1), 47.8 (C-1'). IR/cm^{-1}: 3272, 1646, 1318, 1060. HRMS: found 208.11797 $[C_8H_{17}NO_5+H]^+$, calculated for $[C_8H_{17}NO_5+H]^+$ 208.11795.

N-[5-(Nonyloxy)pentyl]-L-*gluco*-1-deoxynojimycin (167):



161 was subjected to the general procedure A and generated **167** (31 mg, 0.08 mmol) in a yield of 26%. ^{1}H NMR (400 MHz, MeOD) δ 4.21 (d, *J* = 12.5 Hz, 1H, H-6a), 4.00 (dd, *J* = 12.5, 3.2 Hz, 1H, H-6b), 3.80 (ddd, *J* = 11.2, 9.3, 4.9 Hz, 1H, H-2), 3.70 (dd, *J* = 10.5 Hz, 1H, H-4), 3.54 (t, *J* = 12.7 Hz, 2H, H-5'), 3.53 (t, *J* = 12.6 Hz, 2H, H_2-6'), 3.60 – 3.43 (m, 3H, H-1a, H-1'a, H-3), 3.31 (td, *J* = 12.6, 5.3 Hz, 1H, H-1'b), 3.17 (dd, *J* = 10.3, 2.8 Hz, H-5, 1H), 3.10 (dd, *J* = 12.2, 11.2 Hz, 1H, H-1b), 1.96 – 1.81 (m, 2H, H_2-2'), 1.79 – 1.69 (m, 2H, H_2-7'), 1.69 – 1.61 (m, 2H, H_2-4'), 1.59 – 1.50 (m, 2H, H_2-3'), 1.50 – 1.30 (m, 12H, H_2-8' – H_2-13'), 0.94 (t, *J* = 7.0 Hz, 3H, H_3-14'). ^{13}C NMR (100 MHz, MeOD) δ 78.9 (C-3), 72.9 (C-6'), 72.2 (C-5'), 69.7 (C-4), 68.7 (C-2), 68.3 (C-5), 55.7 (C-6), 55.7 (C-1), 55.2 (C-1'), 49.9, 33.9, 31.6, 31.6, 31.5, 31.3, 31.0, 28.1, 25.4, 24.8, 24.6 (C-2' – C-4', C-7' – C-13'), 15.3 (C-14'). $[\alpha]^{20}_D$ = +1.6 (c = 1, MeOH). IR/cm^{-1}:3327, 2955, 2854, 1628, 1456, 1101, 1028. HRMS: found 376.30587 $[C_{20}H_{41}NO_5+H]^+$, calculated for $[C_{20}H_{41}NO_5+H]^+$ 376.30575.

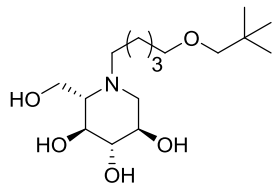
N-[5-(Hexyloxy)pentyl]-L-*gluco*-1-deoxynojimycin (168):



161 was subjected to the general procedure A and generated **168** (12 mg, 0.04 mmol) in a yield of 10%. ^{1}H NMR (400 MHz, MeOD) δ 4.02 (dd, *J* = 12.2, 2.5 Hz, 1H, H-6a), 3.97 (dd, *J* = 12.1, 2.8 Hz, 1H, H-6b), 3.64 (ddd, *J* = 10.7, 7.6, 4.6 Hz, 1H, H-2), 3.52 (t, *J* = 6.4 Hz, 2H, H-5'), 3.51 (t, *J* = 6.6 Hz, 2H, H_2-6'), 3.56 – 3.52 (m, 1H, H-4), 3.31 (t, *J* = 9.1 Hz, 1H, H-3), 3.23 (dd, *J* = 11.6, 4.9 Hz, 1H, H-1a), 3.14 – 3.00 (m, 1H, H-1'a), 2.96 – 2.82 (m, 1H, H-1'b), 2.61 – 2.45 (m, 2H, H-1b, H-5), 1.77 – 1.59 (m, 6H, H_2-2', H_2-7', H_2-4'), 1.54 – 1.34 (m, 8H, H_2-3', H_2-8', H_2-9', H_2-10'), 0.94 (t, *J* = 7.0 Hz, 3H, H_3-11'). ^{13}C NMR (100 MHz, MeOD) δ 80.6 (C-3), 72.8 (C-6'), 72.5 (C-5'), 71.7 (C-4), 70.6 (C-2), 68.2 (C-5), 58.9 (C-6), 57.6

(C-1), 54.7 (C-1'), 33.7, 31.6, 31.3, 27.8, 25.8, 25.5, 24.5 (C-2' – C-4', C-7' – 10'), 15.3 (C-11'). $[\alpha]^{20}_{D}$ = +9.0 (c = 0.2, MeOH). IR/cm^{-1}: 3361, 2933, 2860, 1670, 1456, 1375, 1202, 1101, 1034. HRMS: found 334.25897 $[C_{17}H_{35}NO_5+H]^+$, calculated for $[C_{17}H_{35}NO_5+H]^+$ 334.25880.

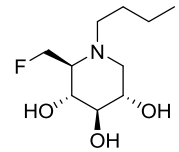
N-[5-(3,3-Dimethyl-1-propyloxy)pentyl]-L-*gluco*-1-deoxynojimycin (169):



161 was subjected to the general procedure A and generated **169** (63 mg, 0.19 mmol) in a yield of 33%. ^{1}H NMR (400 MHz, MeOD) δ 4.06 (dd, *J* = 12.2, 2.2 Hz, 1H, H-6a), 3.98 (dd, *J* = 12.2, 3.0 Hz, 1H, H-6b), 3.67 (td, *J* = 10.5, 9.9, 4.8 Hz, 1H, H-2), 3.56 (t, *J* = 9.7 Hz, 1H, H-4), 3.53 (t, *J* = 6.3 Hz, 2H, H_2-5'), 3.34 (t, *J* = 9.1 Hz, 1H, H-3), 3.38 – 3.27 (m, 1H, H-1a), 3.16 (s, 2H, H_2-6'), 3.16 (br s, 1H, H-1'a), 2.67 (br s, 2H, H-1b, H-5), 1.85 – 1.66 (m, 4H, H_2-2', H_2-4'), 1.59 – 1.43 (m, 2H, H_2-3'), 0.93 (s, 9H, H_3-8', H_3-9', H_3-10'). ^{13}C NMR (100 MHz, MeOD) δ 83.4 (C-6'), 80.3 (C-3), 73.1 (C-5'), 71.3 (C-4), 70.2 (C-2), 68.2 (C-5), 58.6 (C-6), 56.3 (C-1), 54.8 (C-1'), 33.8 (C-7'), 31.3 (C-4'), 28.0 (C-8',C-9',C-10'), 25.8 (C-3'), 25.4 (C-2'). $[\alpha]^{20}_{D}$ = +7.2 (c = 1, MeOH). IR/cm^{-1}: 3280, 2951, 2862, 1734, 1637, 1458, 1387, 1362, 1113, 1032. HRMS: found 320.24339 $[C_{16}H_{33}NO_5+H]^+$, calculated for $[C_{16}H_{33}NO_5+H]^+$ 320.24315.

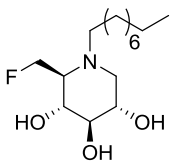
C-6 fluorinated DNJ derivatives

N-Butyl-1,6-dideoxy-6-fluoro-1,5-imino-D-glucitol (177):



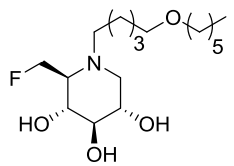
1-Bromobutane (0.375 mmol) was subjected to general procedure A with 1,5,6-trideoxy-6-fluoro-1,5-imino-D-glucitol (0.25 mmol) to provide **177.** ^{1}H NMR (400 MHz, MeOD) δ 5.04 (qd, *J* = 12.0, 2.4 Hz, 1H, H-6a), 4.92 – 4.88 (m, 1H, H-6b), 3.74 (td, *J* = 10.6, 10.1, 4.7 Hz, 1H, H-2), 3.65 – 3.56 (m, 1H, H-4), 3.54 (dd, *J* = 12.2, 4.8 Hz, 1H, H-1a), 3.44 (t, *J* = 9.2 Hz, 1H, H-3), 3.41 – 3.32 (m, 2H, H-1'a, H-5), 3.23 (td, *J* = 12.2, 5.2 Hz, 1H, H-1'b), 3.04 (t, *J* = 11.6 Hz, 1H, H-1b), 1.81 – 1.66 (m, 2H, H_2-2'), 1.48 – 1.40 (m, 2H, H_2-3'), 1.00 (t, *J* = 7.4 Hz, 3H, H_3-4'). ^{13}C NMR (100 MHz, MeOD) δ 78.6 (d, J_{CF} = 170.0 Hz, C-6), 77.0 (C-3), 68.5 (C-4), 67.7 (C-2), 66.4 (d, J_{CF} = 17.7 Hz, C-5), 55.1 (C-1), 54.6 (C-1'), 26.2 (C-2'), 20.8 (C-3'), 13.8 (C-4'). IR/cm^{-1}: 3208, 2909, 1663, 1437, 1184, 1132, 1055, 1024. HRMS: found 222.14995 $[C_{10}H_{20}FNO_3+H]^+$, calculated for $[C_{10}H_{20}FNO_3+H]^+$ 222.15000.

N-Nonyl-1,6-dideoxy-6-fluoro-1,5-imino-D-glucitol (178):



1-Bromononane (0.375 mmol) was subjected to general procedure A with 1,5,6-trideoxy-6-fluoro-1,5-imino-D-glucitol (0.25 mmol) to provide **178**. ^{1}H NMR (400 MHz, MeOD) δ 5.05 (ddd, *J* = 12.8, 12.3, 2.4 Hz, 1H, H-6a), 4.97 – 4.90 (m, 1H, H-6b), 3.72 (ddd, *J* = 10.5, 10.0, 4.7 Hz, 1H, H-2), 3.59 (t, *J* = 9.5 Hz, 1H, H-4), 3.52 (dd, *J* = 12.2, 4.8 Hz, 1H, H-1a), 3.43 (t, *J* = 8.9 Hz, 1H, H-3), 3.40 – 3.34 (m, 2H, H-1'a, H-5), 3.21 (td, *J* = 12.4, 5.4 Hz, 1H, H-1'b), 3.03 (t, *J* = 11.6 Hz, 1H, H-1b), 1.80 – 1.70 (m, 2H, H_2-2'), 1.47 – 1.19 (m, 12H, H_2-3', H_2-4', H_2-5', H_2-6', H_2-7', H_2-8'), 0.90 (t, *J* = 6.6 Hz, 3H, H_3-9'). ^{13}C NMR (100 MHz, MeOD) δ 78.6 (d, J_{CF} = 168.8 Hz, C-6), 77.1 (C-3), 68.6, 68.5 (C-4), 67.8 (C-2), 66.4 (d, J_{CF} = 17.8 Hz, C-5), 54.8 (C-1), 54.4 (C-1'), 32.9, 30.4, 30.2, 30.2, 27.6, 24.3, 23.6 (C-2' – C-8'), 14.4 (C-9'). IR/cm^{-1}: 3244, 2926, 2857, 1666, 1456, 1435, 1200, 1184, 1086, 1022. HRMS: found 292.22803 $[C_{15}H_{30}FNO_3+H]^+$, calculated for $[C_{15}H_{30}FNO_3+H]^+$ 292.22825.

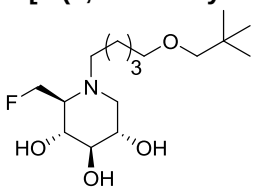
N-[5-(Hexyloxy)pentyl]-1,6-dideoxy-6-fluoro-1,5-imino-D-glucitol (179):



Pentyloxyhexyl bromide (0.375 mmol) was subjected to general procedure A with 1,5,6-trideoxy-6-fluoro-1,5-imino-D-glucitol (0.25 mmol) to provide **179**. ^{1}H NMR (400 MHz, MeOD) δ 5.11 – 4.89 (m, 2H, H_2-6), 3.70 (ddd, *J* = 14.4, 8.6, 4.4 Hz, 1H, H-2), 3.58 (t, *J* = 9.9 Hz, 1H, H-

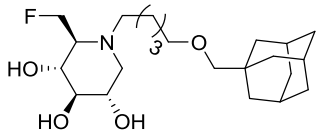
4), 3.50 (dd, *J* = 12.2, 4.8 Hz, 1H, H-1a), 3.46 (t, *J* = 6.2 Hz, 2H, H_2-5'), 3.43 (t, *J* = 6.6 Hz, 2H, H_2-6'), 3.41 – 3.29 (m, 3H, H-3, H-1'a, H-5), 3.21 (td, *J* = 12.2, 5.1 Hz, 1H, H-1'b), 3.00 (t, *J* = 11.5 Hz, 1H, H-1b), 1.84 – 1.74 (m, 2H, H_2-2'), 1.69 – 1.60 (m, 2H, H_2-4'), 1.58 – 1.53 (m, 2H, H_2-7'), 1.48 – 1.45 (m, 2H, H_2-3'), 1.40 – 1.23 (m, 6H, H_2-8', H_2-9', H_2-10'), 0.93 (t, *J* = 7.0 Hz, 3H, H_3-11'). ^{13}C NMR (100 MHz, MeOD) δ 78.6 (d, J_{CF} = 174.4 Hz, C-6), 72.1 (C-6'), 71.4 (C-5'), 68.7 (C-4), 67.9 (C-2), 66.4 (d, J_{CF} = 17.7 Hz, C-5), 54.7 (C-1), 54.6 (C-1'), 32.8, 30.7, 30.1, 26.9, 24.4, 24.2, 23.6 (C-2' – C-4', C-7' – C-10'), 14.4 (C-11'). IR/cm^{-1}: 3310, 2934, 2860, 2800, 1670, 1456, 1435, 1377, 1204, 1134, 1022, 839, 800, 723. HRMS: found 336.25416 $[C_{17}H_{34}FNO_4+H]^+$, calculated for $[C_{17}H_{34}FNO_4+H]^+$ 336.25446.

N-[5-(3,3-Dimethyl-1-propyloxy)pentyl]-1,6-dideoxy-6-fluoro-1,5-imino-D-glucitol (180):



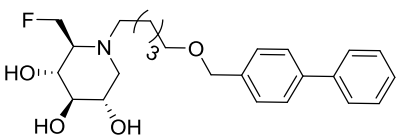
1-Bromo-5-(2,2-dimethyl-1-propoxy) pentane (0.375 mmol) was subjected to general procedure A with 1,5,6-trideoxy-6-fluoro-1,5-imino-D-glucitol (0.25 mmol) to provide **180**. ^{1}H NMR (400 MHz, MeOD) δ 5.11 – 4.86 (m, 2H, H_2-6), 3.71 (td, *J* = 10.5, 4.7 Hz, 1H, H-2), 3.59 (t, *J* = 9.2 Hz, 1H, H-4), 3.52 (dd, *J* = 12.2, 4.8 Hz, 1H, H-1a), 3.45 (t, *J* = 6.2 Hz, 2H, H_2-5'), 3.43 – 3.34 (m, 3H, H-1'a, H-3, H-5), 3.23 (ddd, *J* = 12.7, 12.3, 5.2 Hz, 1H, H-1b), 3.08 (s, 2H, H_2-6'), 3.03 (t, *J* = 11.6 Hz, 1H, H-1b), 1.90 – 1.70 (m, 2H, H_2-2'), 1.65 (dt, *J* = 8.0, 6.4 Hz, 2H, H_2-4'), 1.54 – 1.36 (m, 2H, H_2-3'), 0.90 (s, 9H, H_3-8', H_3-9', H_3-10'). ^{13}C NMR (100 MHz, MeOD) δ 82.5 (C-6'), 78.48 (d, J_{CF} = 174.2 Hz, C-6) 78.1 (C-3), 72.0 (C-5'), 68.6 (C-4), 67.8 (C-2), 66.38 (d, J_{CF} = 17.8 Hz, C-5), 54.8 (C-1), 54.7 (C-1'), 32.9 (C-7'), 30.1 (C-4'), 27.1 (C-8', 9', 10'), 24.9 (C-3'), 24.4 (C-2'). IR/cm^{-1}: 3302, 2955, 2866, 1670, 1435, 1387, 1364, 1204, 1136, 1026. HRMS: found 322.23860 $[C_{16}H_{32}FNO_4+H]^+$, calculated for $[C_{16}H_{32}FNO_4+H]^+$ 322.23881.

N-[5-(Adamantan-1-yl-methoxy)pentyl]-6-fluoro-1,5-imino-D-glucitol (181):



5-(Adamantan-1-yl-methoxy)pentyl bromide (0.375 mmol) was subjected to general procedure A with 1,5,6-trideoxy-6-fluoro-1,5-imino-D-glucitol (0.25 mmol) to provide **181.** ^{1}H NMR (400 MHz, MeOD) δ 3.70 (td, *J* = 10.5, 4.7 Hz, 1H, H-2), 3.54 (t, *J* = 9.5 Hz, 1H, H-4), 3.44 (dd, *J* = 12.4, 5.0 Hz, 1H, H-1a), 3.39 (t, *J* = 9.1 Hz, 1H, H-3), 3.31 (t, *J* = 6.2 Hz, 2H, H_2-5'), 3.33 – 3.20 (m, 2H, H-5, H-1'a), 3.13 (ddd, *J* = 12.8, 12.3, 5.3 Hz, 1H, H-1'b), 2.93 (t, *J* = 11.6 Hz, 1H, H-1b), 2.88 (s, 2H, H_2-6'), 1.85 (t, *J* = 3.4 Hz, 3H, 3 x CH ada), 1.76 – 1.63 (m, 2H, H_2-2'), 1.65 – 1.52 (m, 8H, 3 x CH_2 ada, H_2-4'), 1.44 (d, *J* = 3.0 Hz, 6H, 3 x CH_2 ada), 1.41 – 1.23 (m, 2H, H_2-3'). ^{13}C NMR (100 MHz, MeOD) δ 82.7 (C-6'), 78.6 (d, J_{CF} = 170.7 Hz, C-6), 77.0 (C-3), 71.7 (C-5'), 68.1 (C-4), 67.1 (C-2), 65.97 (d, J_{CF} = 17.8 Hz, C-5), 54.5 (C-1), 54.5 (C-1'), 40.4 (CH_2 ada), 37.9 (CH_2 ada), 34.8 (C_q ada), 29.6 (C-4'), 29.2 (CH ada), 24.0 (C-3'), 23.6 (C-2'). IR/cm^{-1}: 3354, 2901, 2847, 2590, 1651, 1446, 1205, 1184, 1140, 1018. HRMS: found 400.28468 $[C_{22}H_{38}FNO_4+H]^+$, calculated for $[C_{22}H_{38}FNO_4+H]^+$ 400.28576.

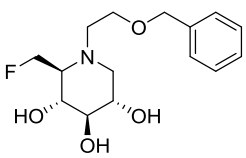
N-[(Biphenyl-4-yl-methoxy)pentyl]-6-fluoro-1,5-imino-D-glucitol (182):



(Biphenyl-4-yl-methoxy)-pentyl bromide (0.375 mmol) was subjected to general procedure A with 1,5,6-trideoxy-6-fluoro-1,5-imino-D-glucitol (0.25 mmol) to provide **182**. ^{1}H NMR (400 MHz, MeOD) δ 7.61 (d, *J* = 7.9 Hz, 4H, H_{Ar} BiPh), 7.47 – 7.31 (m, 5H, H_{Ar} BiPh), 5.12 – 4.75 (m, 2H, H_2-6), 4.55 (s, 2H, H_2-6'), 3.70 (td, *J* = 10.0, 4.5 Hz, 1H, H-2), 3.57 (t, *J* = 6.2 Hz, 2H, H_2-5'), 3.51 (dd, *J* = 12.2, 4.9 Hz, 1H, H-4), 3.45 – 3.30 (m, 3H, H-1a, H-3, H-1'a), 3.23 (ddd, *J* = 13.1, 12.5, 5.7 Hz, 1H, H-1'b), 3.02 (t, *J* = 11.6 Hz, 1H, H-1b), 1.89 – 1.75 (m, 2H, H_2-2'), 1.76 – 1.66 (m, 2H, H_2-4'), 1.61 – 1.44 (m, 2H, H_2-3'). ^{13}C NMR (100 MHz, MeOD) δ 142.0, 138.7 (C_q BiPh), 129.9 – 127.9 (C_{Ar} BiPh), 78.4 (d, J_{CF} = 169.5 Hz, C-6), 77.9 (C-3), 73.7 (C-6'), 71.0 (C-5'), 68.5 (C-4), 67.8 (C-2), 66.3 (d, J_{CF} = 17.7 Hz, C-5), 54.9 (C-1), 54.7 (C-1'), 30.0 (C-4'), 24.5 (C-3'), 24.0 (C-2'). IR/cm^{-1}:

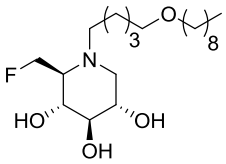
3304, 2918, 2864, 1672, 1487, 1435, 1364, 1203, 1134, 1022, 841. HRMS: found 418.23818 $[C_{24}H_{32}FNO_4+H]^+$, calculated for $[C_{24}H_{32}FNO_4+H]^+$ 418.23881.

_N_-(Benzyloxy)ethyl-1,6-dideoxy-6-fluoro-1,5-imino-D-glucitol (183):



(2-Benzyloxy)ethyl bromide (0.375 mmol) was subjected to general procedure A with 1,5,6-trideoxy-6-fluoro-1,5-imino-D-glucitol (0.25 mmol) to provide **183**. ^{1}H NMR (400 MHz, MeOD) δ 7.38 – 7.25 (m, 5H, H_{Ar} Bn), 5.25 – 4.90 (m, 2H, H_2-6), 4.59 (s, 2H, CH_2 Bn), 3.85 (t, *J* = 4.9 Hz, 2H, H_2-2'), 3.78 – 3.61 (m, 2H, H-2, H-1'a), 3.60 – 3.55 (m, 2H, H-4, H-1a), 3.49 (dt, *J* = 14.1, 4.9 Hz, 1H, H-1'b), 3.39 (t, *J* = 9.0 Hz, 1H, H-3), 3.05 (t, *J* = 11.6 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, MeOD) δ 138.5 (C_q Bn), 129.6 – 129.2 (CH_{Ar} Bn), 78.8 (d, J_{CF} = 169.1 Hz, C-6), 74.4 (C-3'), 68.5 (C-4), 67.8 (C-2), 66.2 (d, J_{CF} = 17.6 Hz, C-5), 64.6 (C-2'), 55.6 (C-1), 54.2 (C-1'). IR/cm^{-1}: 3235, 2874, 1670, 1456, 1437, 1364, 1202, 1134, 1026. HRMS: found 300.16042 $[C_{15}H_{22}FNO_4+H]^+$, calculated for $[C_{15}H_{22}FNO_4+H]^+$ 300.16056.

_N_-(Nonyloxy)pentyl-1,6-dideoxy-6-fluoro-1,5-imino-D-glucitol (184):



Pentyloxynonyl bromide was subjected to general procedure A with 1,5,6-trideoxy-6-fluoro-1,5-imino-D-glucitol (0.25 mmol) to provide **184**. ^{1}H NMR (400 MHz, Methanol-d_4) δ 5.05 (ddd, *J* = 11.0, 10.2, 2.3 Hz, 1H, H-6a), 4.99 – 4.92 (m, 1H, H-6b), 3.71 (ddd, *J* = 10.9, 9.0, 4.8 Hz, 1H, H-2), 3.59 (t, *J* = 9.6 Hz, 1H, H-4), 3.52 (dd, *J* = 12.2, 4.8 Hz, 1H, H-1a), 3.46 (t, *J* = 6.1 Hz, 2H, H_2-5'), 3.43 (t, *J* = 6.5 Hz, 2H, H_2-6'), 3.40 – 3.30 (m, 3H, H-3, H-1'a, H-5), 3.22 (ddd, *J* = 12.7, 12.3, 5.2 Hz, 1H, H-1'b), 3.02 (t, *J* = 11.6 Hz, 1H, H-1b), 1.89 – 1.69 (m, 2H, H_2-2'), 1.73 – 1.62 (m, 2H, H_2-4'), 1.63 – 1.53 (m, 2H, H_2-7'), 1.53 – 1.42 (m, 2H, H_2-3'), 1.38 – 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* = 6.8 Hz, 3H, H_2-14'). ^{13}C NMR (100 MHz, MeOD) δ 78.6 (d, *J* = 168.3 Hz, C-6), 72.1 (C-6'), 71.4 (C-5'), 77.2 (C-3), 68.6 (C-4), 67.8 (C-2), 66.4 (d, *J* = 17.7 Hz, C-5), 55.1 (C-1), 54.7 (C-1'), 33.0, 30.7, 30.6, 30.4, 30.1, 27.2, 24.4, 24.1, 23.7 (C-2' – C-4', C-7' – C-13'), 14.4 (C-14'). IR/cm^{-1}: 3294, 2926, 2855, 1670, 1458, 1437, 1202, 1132, 1022. HRMS: found 378.30158 $[C_{20}H_{40}FNO_4+H]^+$, calculated for $[C_{20}H_{40}FNO_4+H]^+$ 378.30141.

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