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

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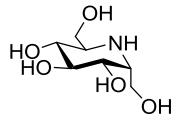
3 Synthesis of Glycosylated 1-Deoxynojirimycin

Introduction

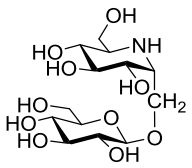
Iminosugars have received considerable interest in the past decades because of their potential to inhibit glycosidases and glycosyl transferases. A relatively unexplored class of iminosugars comprises the glycosylated deoxynojirimycin derivatives. Whereas monosaccharide analogues act as exoglycosidase inhibitors and sometimes also as glycosyl transferase inhibitors, iminosugars functionalized with a monosaccharide or an oligosaccharide may well act as inhibitors of another major class of glycoprocessing enzymes: endoglycosidases.

The glycosylated iminosugar, MDL25637 (**2**), is a relevant example of the potential of this class of compounds. It is a potent trehalase inhibitor (which is an established target for the treatment of type 2 diabetes), in contrast to the corresponding monosaccharide iminosugar, α-homonojirimycin (**1**), which does not inhibit this endoglycosidase activity.[1]

***Figure 1**: Structure of α-homonojirimycin and MDL25637*



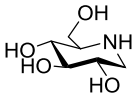
1, α-homonojirimycin



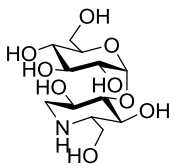
2, MDL25637

Glycosylated iminosugars have been isolated from plants and microorganisms, often organisms that also produce DNJ. However, their natural abundance is usually rather low. For instance, in order to isolate 50 mg of α-glucosylated deoxynojirimycin **4** (Figure 2), 50 kg of mulberry tree root bark is required.[2] The synthesis of glycosylated DNJ derivatives is therefore an attractive alternative. Three conceptual approaches can be discerned by means of which glycosylated DNJ have been prepared. These are 1) enzymatic glycosylation of DNJ derivatives, 2) chemical glycosylation of DNJ derivatives and 3) strategies based on disaccharide entities as starting material.

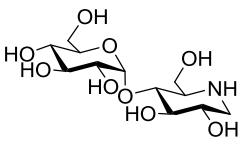
***Figure 2**: Structure of DNJ and glucosylated DNJ derivatives*



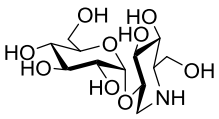
3, DNJ



4



5, *malto*-DNJ



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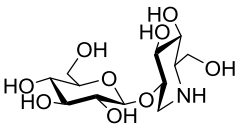

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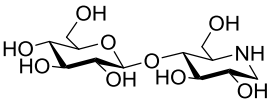
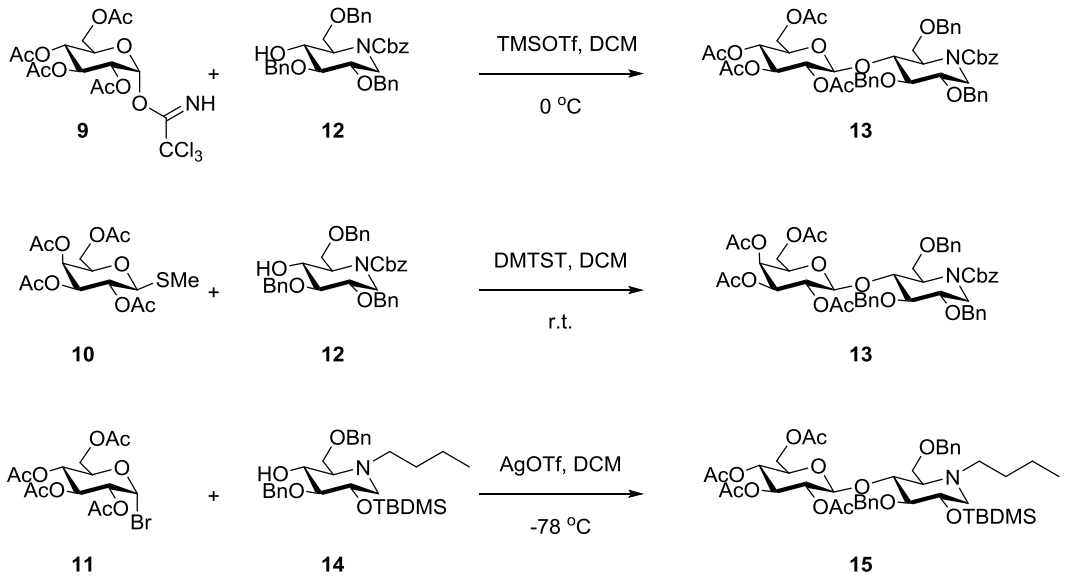


8, *cellobio*-DNJ

The enzymatic glycosylation of DNJ derivatives has been accomplished using glycohydrolases as catalysts in transglycosylation events using an appropriate donor glycoside. One of the earliest endeavors in this vein comprises the synthesis of compound **5** (Figure 2)

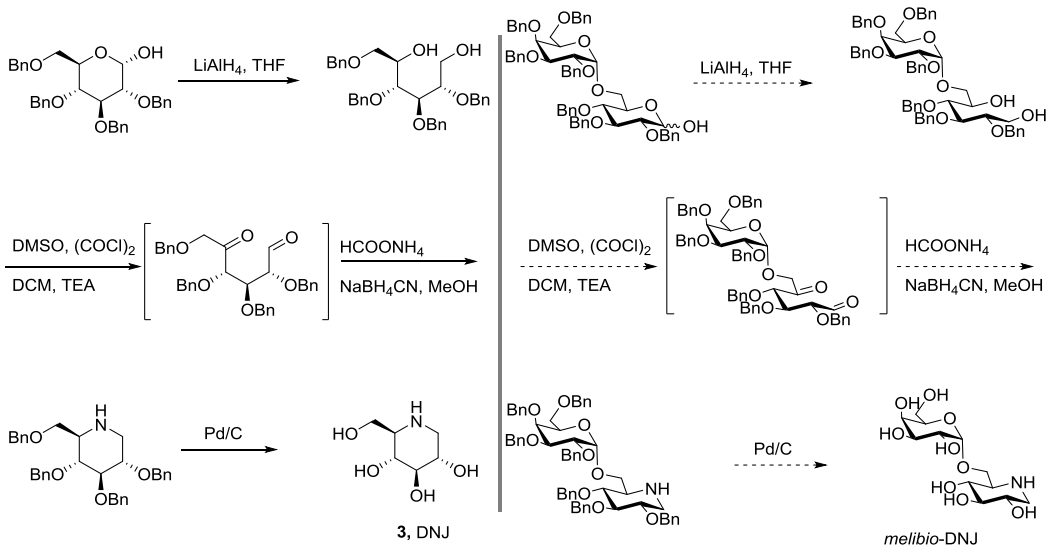
using α-cyclodextrin as glucose donor and *bacillus macerans* amylase as transglycosylase.[3] Following these studies, it was shown that a variety of alternative glycosides including *p*-nitrophenyl-α-D-galactose,[4] UDP-glucose,[5] and lactose[6] are effective donor glycosides as well, expanding the methodology to yield a variety of glycosylated DNJ derivatives. Besides glycosidases also glycosyl transferases have been recruited in the enzymatic synthesis of glycosylated DNJ derivatives. Enzymatic approaches hold several advantages, including mild reaction conditions, readily available starting material and short reaction sequences. However, enzymatic synthesis also has its limitations, including structural diversity that can be obtained in general and, in particular in the use of transglycosylations, the potential formation of structural isomers. For example, when cellobiose was chosen as glycosyl donor and yeast β-glucosidase as the transglycosylase catalyst, **4**, **6**, **7** and **8** (Figure 2) as well as a number of other oligosaccharides were formed as a mixture.[7] Because of their similar chemical and physical properties, separation of such a mixture of glycosylated iminosugars can be a challenge.

***Scheme 1**: Examples of chemical glycosylations of DNJ*



Chemical glycosylation forms an attractive alternative for enzymatic glycosylation of DNJ. In chemical glycosylation approaches, part of the hydroxyl groups in the acceptor (in this case, DNJ) are selectively protected, leaving the hydroxyl to be modified free for glycosylation using an appropriate donor (1-trichloroacetimidate **9,**[8] 1-thioglycoside **10**[9] or 1-bromoglycoside **11,**[10] scheme 1) and activation strategy. Since the synthesis of a donor and acceptor may take quite a few protection and deprotection steps, this strategy may be – compared to enzymatic synthesis - somewhat lengthy and tedious.

***Scheme 2**: Synthesis of DNJ[11] and proposed synthesis of melibio-DNJ via double reductive amination.*



The third conceptual strategy towards glycosylated DNJ derivatives that has been studied to some extent comprises the use of disaccharides as starting material. In this strategy multistep preparation of the donor and acceptor moieties is avoided, but the caveat is that appropriate disaccharide starting materials should be available. The transformation of disaccharides into glycosylated DNJ derivatives described in this chapter is rooted in the double reductive amination strategy (Scheme 2, *melibio*-DNJ as example) by means of which a partially protected glucitol, in which the C-1 and C-5 alcohols are free for modification, can be transformed into DNJ (see for details on this strategy also Chapter 2). In this strategy, the anomeric center of a partially protected disaccharide is selectively exposed, and the hemi-acetal reduced to generate the key 1,5-diol intermediate. This diol is oxidized to the keto-aldehyde, which in a double reductive amination event to produce the target glycosylated DNJ derivative. An important feature of this scheme is the recovery of the stereocenter at C-5 of the newly formed iminosugar, which works well when the glucopyranose configuration is the desired one.

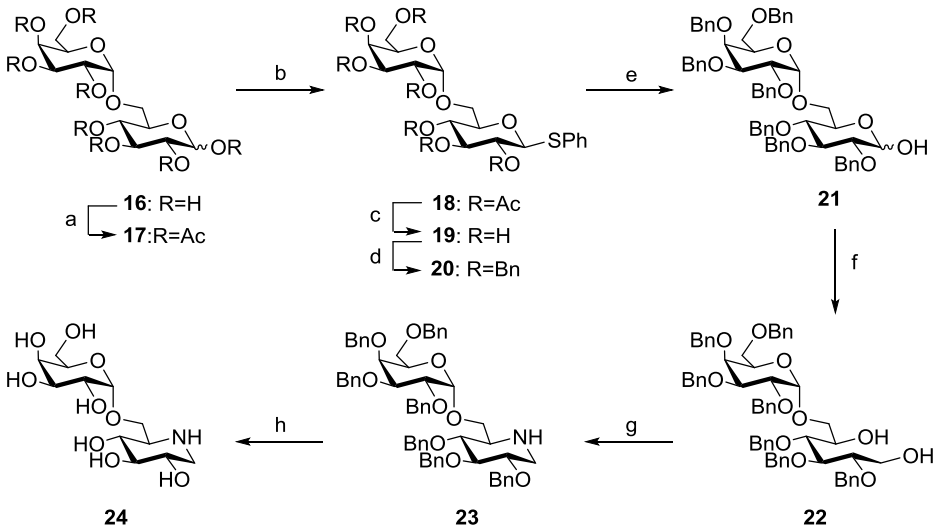
Results and discussion

Synthesis of 6-*O*-(α-D-galactopyranosyl)-1-deoxynojirimycin (24)

The synthesis of 6-*O*-(α-D-galactopyranosyl)-1-deoxynojirimycin **24** (*melibio*-DNJ) commences from melibiose **16**, which is commercially available. Treatment of **16** with sodium acetate in refluxing acetic anhydride afforded peracetylated melibiose **17**, which was reacted with thiophenol and $BF_3{\cdot}Et_2O$ to give thiophenyl melibioside **18**[12] in 74% yield over the two

steps. Zémplen deacetylation followed by benzylation yielded perbenzylated thiomelibiose **20**, the thiolphenyl group in which could be removed using literature conditions[13] (treatment with *N*-iodosuccinimide and trifluoroacetic acid) to yield lactol **21** as the key intermediate in 39% yield over the three steps.

***Scheme 3**: Syntheses of **24** from melibiose*

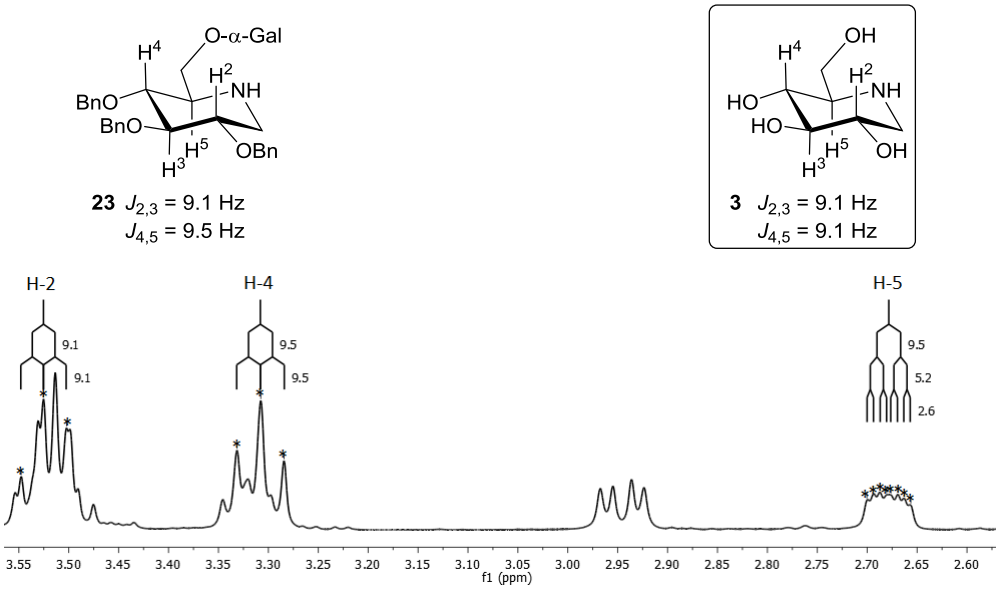


Reagents and conditions: [**a**] Ac_2O, NaOAc, reflux, 90%; [**b**] $BF_3{\cdot}Et_2O$, PhSH, DCM, 82%; [**c**] NaOMe, MeOH; [**d**] BnBr, NaH, DMF, 50% 2 steps; [**e**] NIS, TFA, DCM, 77%; [**f**] $LiAlH_4$, THF, 74%; [**g**] 1) $(COCl)_2$, DMSO; 2) $HCOONH_4$, Na_2SO_4, $NaBH_3CN$, 71% 2 steps; [**h**] 10% Pd/C, DMF/MeOH, 1M HCl, 75%.

In the next step, the hemiacetal moiety in **21** was reduced (lithium aluminum hydride) to give diol **22**, which was oxidized to the corresponding keto-aldehyde using Swern conditions. Double reductive amination with concomitant regeneration of the chiral center at C-5 was accomplished using ammonium formate and sodium cyanoborohydride to yield protected 1-*melibio*-deoxynojirimycin **23** (52% yield, three steps). The chirality of carbon C-5 in **23** was unambiguously established by proton NMR, revealing that, as expected, the iminosugar moiety in **23** has the D-*gluco*-configuration (as in DNJ). The coupling constants between H-4 and H-5 (9.5 Hz) and between H-2 and H-3 (9.1 Hz) are in full agreement with the presented stereochemistry of **23**, and the stereochemical outcome of the double reductive amination step is therefore as was observed previously for the synthesis of DNJ using the same sequence of events (reduction of the hemi-acetal in 2,3,4,6-tetra-*O*-benzyl-glucopyranose, followed by Swern oxidation of both primary and secondary alcohol and finally double reductive amination of the intermediate 5-keto-aldehyde, Figure 3, inserted box).[11] Removal of the benzyl groups in

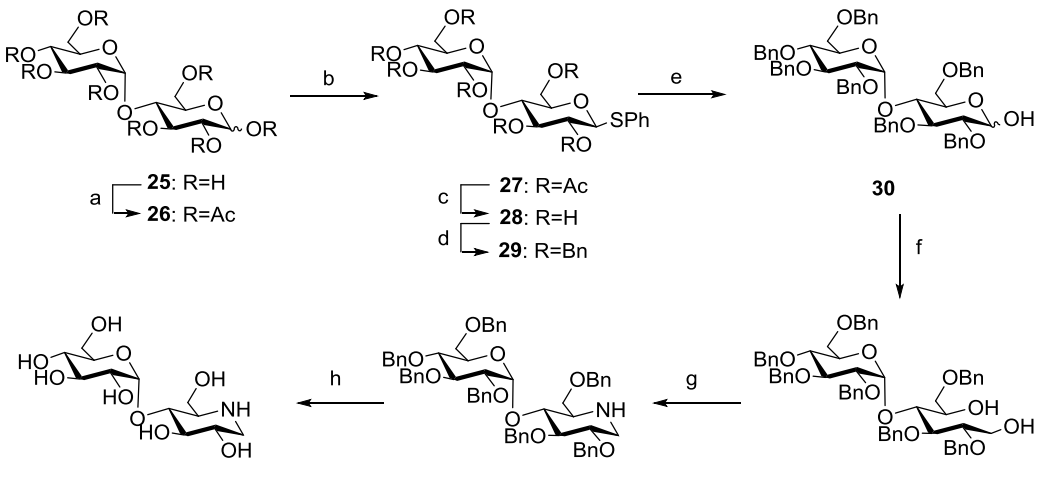
23 by palladium-catalyzed hydrogenation gave the target imino-disaccharide **24** in 11% overall yield starting from **16**.

Figure 3**: Part of the 400 MHz proton NMR spectra of **23



Synthesis of 4-*O*-(α-D-glucopyranosyl)-1-deoxynojirimycin (33)

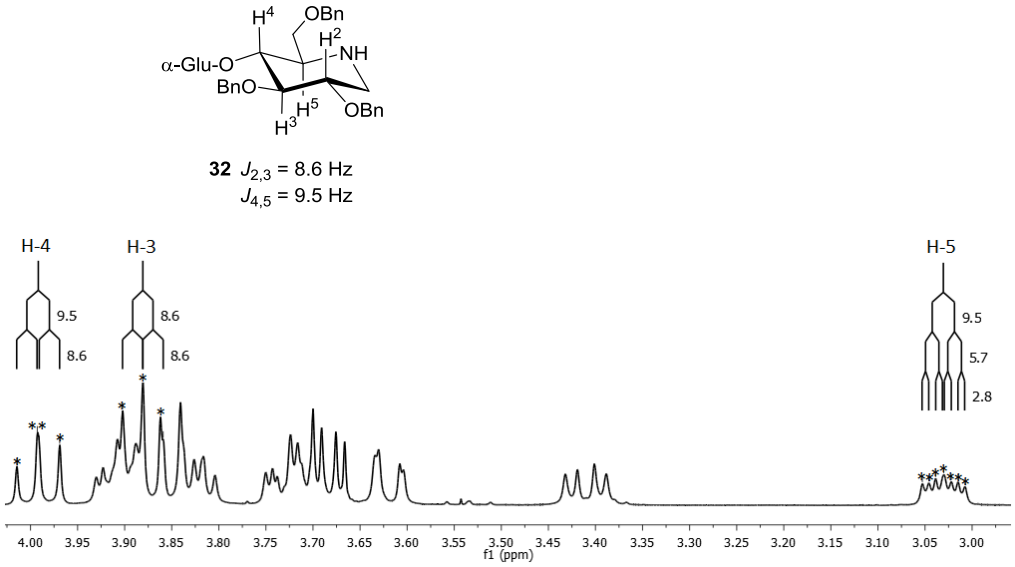
***Scheme 4**: Synthesis of **33** from maltose*



Reagents and conditions: [**a**] Ac_2O, NaOAc, reflux, 94%; [**b**] $BF_3{\cdot}Et_2O$, PhSH, DCM, 61%; [**c**] NaOMe, MeOH; [**d**] BnBr, NaH, DMF, 89%; [**e**] NIS, TFA, DCM, 93%; [**f**] $LiAlH_4$, THF, 74%; [**g**] 1) $(COCl)_2$, DMSO; 2) $CHOONH_4$, Na_2SO_4, $NaBH_3CN$, 44% 2 steps; [**h**] 10% Pd/C, DMF/MeOH, 1M HCl, 71%.

The synthesis strategy applied for the assembly of 4-*O*-(α-D-glucopyranosyl)-1-deoxynojirimycin **33** (*malto*-DNJ) was identical as that described for the synthesis of **24** (*melibio*-DNJ, scheme 3), but now starting from maltose (**25**). Lactol **30** was uneventfully obtained from maltose **25** in a yield of 47% over the five steps. Lithium aluminum hydride reduction of **30** followed by Swern oxidation and double reductive amination produced fully protected *malto*-DNJ **32** (33% yield, three steps). The stereochemical outcome in synthesizing **32** was revealed by proton NMR spectroscopy (Figure 4). The benzyl groups were removed by palladium-catalyzed hydrogenolysis to form target iminosugar **33** in 11% overall yield starting from (**25**).

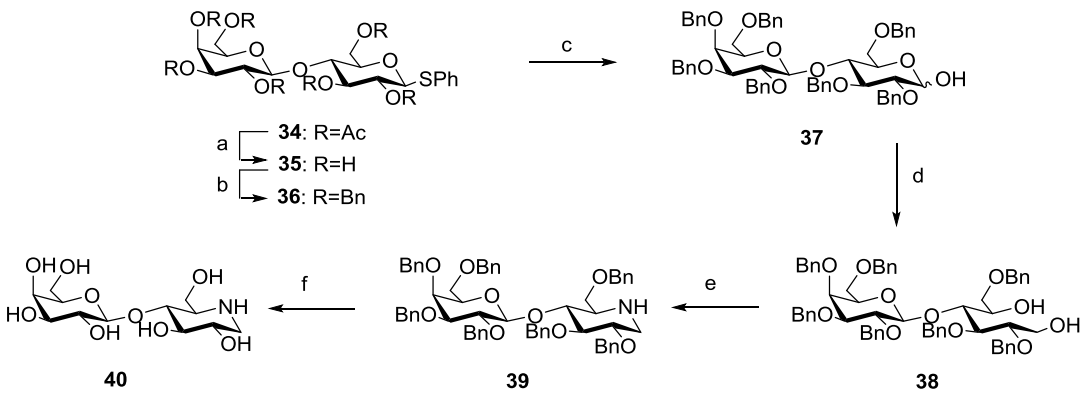
Figure 4**: Part of the 400 MHz proton NMR spectra of **32



Synthesis of 4-*O*-(β-D-galactopyranosyl)-1-deoxynojirimycin (34)

The synthesis of 4-*O*-(β-D-galactopyranosyl)-1-deoxynojirimycin **40** (*lacto*-DNJ) starts with lactose, which is one of the cheapest disaccharide known and is a side product of the dairy industry.[14] Hepta-acetyl thiolactoside **34** was prepared following the sequence of events as described for hepta-acetyl thiomelibioside **18**, but starting from lactose. Compound **34** underwent deacetylation, benzyl protection and NIS/TFA thioglycoside hydrolysis as described before to obtain lactol **37**, and was reduced (lithium aluminum hydride), subjected to Swern oxidation followed by double reductive amination to obtain protected imino-disaccharide **39**. Compound **39** was treated with palladium on carbon and hydrogen gas to give the desired imino-disaccharide **40** in 14% overall yield starting from **34**.

Scheme 5**: Synthesis of **34



Reagents and conditions: [**a**] NaOMe, MeOH; [**b**] BnBr, NaH, DMF, 100% 2 steps; [**c**] NIS, TFA, DCM, 85%; [**d**] $LiAlH_4$, THF, 77%; [**e**] 1) $(COCl)_2$, DMSO; 2) $HCOONH_4$, Na_2SO_4, $NaBH_3CN$, 22%; [**f**] Pd/C, H_2, DMF/MeOH, 64%.

The stereochemistry of carbon C-5 was established by NMR to be as in the parent compound. For comparison, the *J* values between H-2 and H-3 (not changed during the syntheses) and those of H-4 and H-5 (destroyed during Swern oxidation and recovered during reductive amination) of a number of aza-disaccharides discussed in this chapter is given in Table 1.

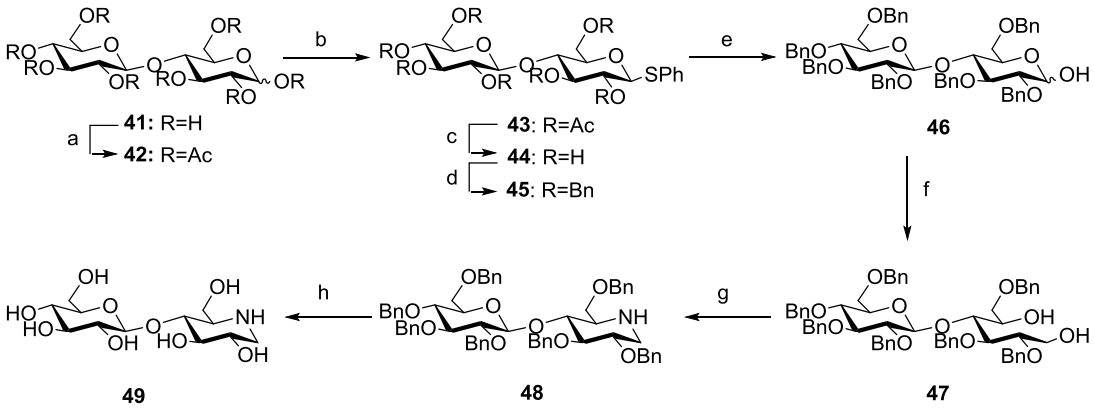
***Table 1:** $J_{2,3}$ and $J_{4,5}$ of DNJ moiety from different molecules*

Molecule	$J_{2,3}$ (Hz)	$J_{4,5}$ (Hz)
1-Deoxynojirimycin (DNJ), **3**	9.1	9.1
Protected *melibio*-DNJ, **23**	9.1	9.5
Protected *malto*-DNJ, **32**	8.6	9.5
Lacto-DNJ, **40**	8.6	9.5
Protected *cellobio*-DNJ, **48**	8.8	9.7
Protected 2-*O*-(α-gal)-DNJ, **68**	9.2	9.3

Synthesis of 4-*O*-(β-D-glucopyranosyl)-1-deoxynojirimycin (49)

Starting from disaccharide cellobiose (**41**), 4-*O*-(β-D-glucopyranosyl)-1-deoxynojirimycin **49** (*cellobio*-DNJ) was obtained in 10% overall yield following the sequence of events as described for the synthesis of **24** (*melobio*-DNJ). The nature of the stereochemistry at C-5 of the thus produced DNJ moiety in **48** was confirmed by NMR spectroscopy (table 1).

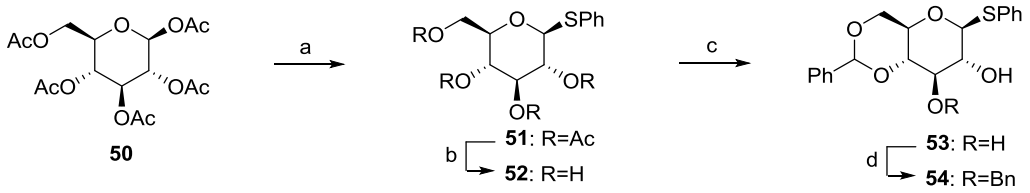
***Scheme 6**: Synthesis of **49** from cellobiose*



Reagents and conditions: [**a**] Ac_2O, NaOAc, reflux, 98%; [**b**] $BF_3{\cdot}Et_2O$, PhSH, DCM, 91%; [**c**] NaOMe, MeOH; [**d**] BnBr, NaH, DMF, 89%; [**e**] NIS, TFA, DCM, 90%; [**f**] $LiAlH_4$, THF, 74%; [**g**] 1) $(COCl)_2$, DMSO; 2) $HCOONH_4$, Na_2SO_4, $NaBH_3CN$, 44% 2 steps; [**h**] 10% Pd/C, DMF/MeOH, 1M HCl, 65%.

Synthesis of 2-*O*-(α-galactopyranosyl)-1-deoxynojirimycin (69)

Scheme 7**: Synthesis of acceptor **54



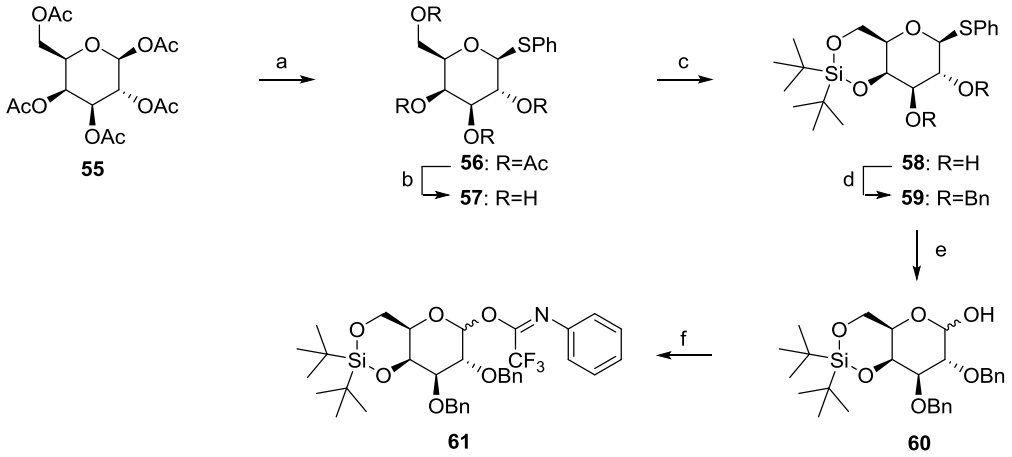
Reagents and conditions: [**a**] $BF_3{\cdot}Et_2O$, PhSH, DCM, 91%; [**b**] NaOMe, MeOH; [**c**] $PhCH(OMe)_2$, *p*-TsOH, DMF, 59% 2 steps; [**d**] Bu_2SnO, TBAI, BnBr, 73%.

The examples described above comprise the use of cheap, readily available disaccharides featuring a glucopyranose moiety at the reducing end as starting material. Obviously, many other disaccharides other than the ones used can be envisaged as starting material and that have a similar lay-out: a glycosylated glucopyranose. Besides making use of available disaccharides of this nature, one can also synthesize these by chemical glycosylation of a partially protected glucopyranose moiety. As an example, partially protected 1-phenylthio-glucopyranoside **54**, with O-2 free for chemical glycosyation, can be prepared following a number of protective group manipulations starting from peracetylated glucopyranose **50** (scheme 7).

Treatment of **50** with borontrifluoride diethyl etherate and thiophenol yielded thiophenylglycoside **51**, the acetyl groups in which were then removed using sodium methoxide to give **52**. The C-4 and C-6 hydroxyls in **52** were protected as the benzylidene acetal, after which regioselective benzylation (dibutyltin oxide, tetrabutylammonion iodide, benzyl bromide) gave **54** in 44% yield over the five steps.

Galactose donor **61** was selected as glycosylating species to functionalize O-2 in **54** prior to its transformation into a DNJ derivative. The synthesis of **61** starts from D-galactose and was accomplished in 7 steps. In the first step, all hydroxyl groups in D-galactose were transformed into the acetates using acetic anhydride and sodium acetate, yielding peracetylated galactopyranose **55**. Treatment of **55** with thiophenol and Lewis acid yielded **56**, which after treatment with sodium methoxide gave thiogalactoside **57**. The C-4 and C-6 hydroxyls in **57** were protected as the di-*tert*-butylsilylene acetal, to yield **58**. The free hydroxyls in **58** were protected as the benzyl ethers (treatment with benzyl bromide and sodium hydride) giving **59**. The thio-acetal linkage in **59** was cleaved (NIS/TFA, **59** to **60**), after which treatment with trifluoro-phenylacetimidoyl chloride gave donor galactoside **61** in an overall yield of 16% starting from galactose.

Scheme 8**: Synthesis of donor **61

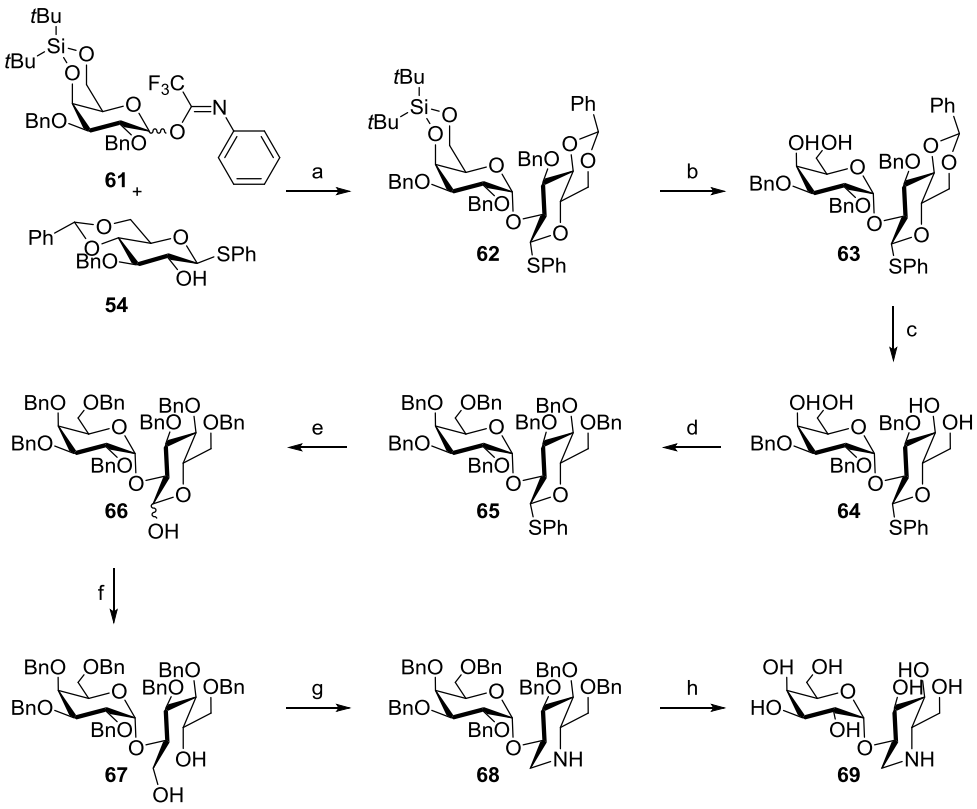


Reagents and conditions: [**a**] $BF_3{\cdot}Et_2O$, PhSH, DCM, 100%; [**b**] NaOMe, MeOH; [**c**] *t*BuSi(OTf)$_2$, 53% 2 steps; [**d**] BnBr, NaH, DMF, 56%; [**e**] NIS, TFA, DCM, 88%; [**f**] trifluoro-phenylacetimidoyl chloride, Cs_2CO_3, acetone, 65%.

Glucose acceptor **54** was next coupled with donor galactoside **61** using trimethylsilyl trifluoromethanesulfonate as the activating agent at 0 °C. Following this methodology, compound **62** was obtained as the main product in good stereoselectivity ($J_{1',2'}$ = 4.0 Hz) in a

yield of 69%. However, when the glycosylation was carried out at -78 °C, the main product proved to be thiophenyl galactopyranoside **59** (yield more than 70%), with no formation of the desired disaccharide **62** observed. When conducting this reaction at -20 °C, **62** was obtained in a yield of 35%, together with a considerable amount of **59** (30%).

Scheme 9**: Synthesis of **69

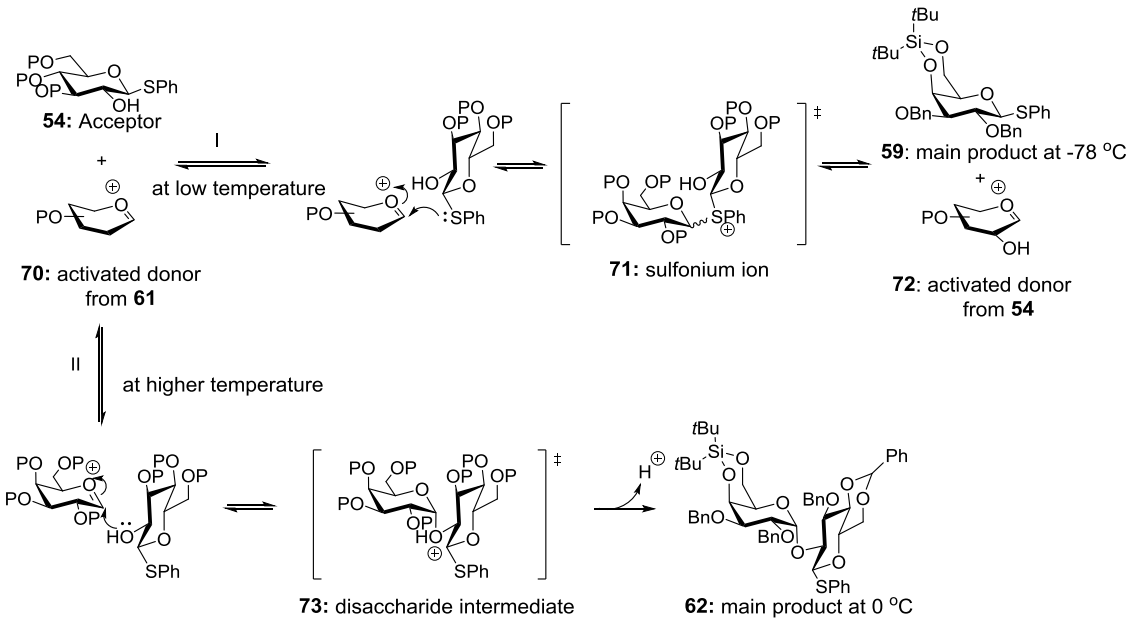


Reagents and conditions: [**a**] TMSOTf, DCM, 0 °C, 69%; [**b**] TBAF, THF, 82%; [**c**] *p*-TsOH, DCM, 90%; [**d**] BnBr, NaH, DMF, 92%; [**e**] NIS, TFA, DCM, 71%; [**f**] $LiAlH_4$, THF, 88%; [**f**] $(COCl)_2$, DMSO, $HCOONH_4$, Na_2SO_4, $NaBH_3CN$, 24%; [g] Pd/C, H_2, EtOH, 1M HCl, 52%.

The generation of **59** at low temperature might be due to the side reaction mechanism visualised in Figure 6. The sulfur and hydroxyl groups on the acceptor can both react with the activated donor, and whether the reaction goes through pathway I or pathway II depends on the relative reactivity of the sulfur and the hydroxyl groups.[15] There exists literature precedents reporting that lowering the temperature favors reaction pathway II and thus avoids the aglycon transfer product.[16-18] However, this is inconsistent with the findings presented here. Arguably, upon formation of oxycarbenium ion **70**, *S*-glycosylation (pathway I) to give sulfonium ion **71**

proceeds easier (thus at lower temperature) than *O*-glycosylation (pathway II) to give protonated disaccharide **73**. Once **73** is formed, however, deprotonation yields the final disaccharide as the thermodynamic end point. Assuming the occurrence of an equilibrium between sulfonium ion **71** and *in situ* formed oxycarbenium ion **70** (and acceptor **54**), and by allowing the formation of **73** as well (by elevating the temperature) the reaction will then proceed towards disaccharide **62**. In case the temperature is insufficiently high to overcome the barrier towards **73**, and therefore allowing only pathway I to occur, eventually expulsion of oxycarbenium ion **72** (which will deteriorate during work-up) may occur as the main conclusive event, delivering phenylthiogalactoside **59**.

***Figure 6**: Chemical glycosylation products at different temperatures*



With disaccharide **62** in hand, the corresponding aza-disaccharide was readily prepared using the sequence of events also used for the preparation of the other aza-disaccharides described in this chapter. In the first instance, the di-*tert*-butylsilylene ester in **62** was removed using tetra-*N*-butylammoniumfluoride (TBAF) to afford **63**. Removal (with *p*-toluenesulfonic acid) of the benzylidene in **63** gave **64** as white crystals (90%) and the free hydroxyls in **64** were benzylated (sodium hydride and benzyl bromide) to give **65**. NIS/TFA mediated hydrolysis of the phenyltio acetal yielded hemi-acetal **66**, which was subjected to $LiAlH_4$ mediated reduction to give diol **67** in a yield of 88%. Subsequent oxidation of both alcohols in **67** followed by the double reductive amination procedure gave protected iminosugar **68**.

Proton NMR spectroscopy of **68** confirmed that the DNJ configuration was obtained also in this instance (see table 1). The benzyl protecting groups in **68** were finally removed to give aza-disaccharide **69** in an overall yield of 7% based on **62**.

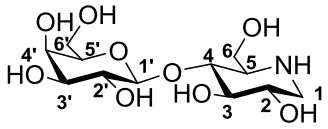
Conclusion

This Chapter reports on the synthesis of five glycosylated 1-deoxynojimycin derivatives. Four of these, namely 6-*O*-(α-D-galactopyranosyl)-1-deoxynojirimycin (**24**), 4-*O*-(α-D-glucopyranosyl)-1-deoxynojirimycin (**33**), 4-*O*-(β-D-glucopyranosyl)-1-deoxynojirimycin (**49**) and 4-*O*-(β-D-galactopyranosyl)-1-deoxynojirimycin (**40**) were synthesized from their commercially available disaccharide (melibiose, maltose, cellobiose and lactose, respectively) as precursor. As a further example, 2-*O*-(α-galactopyranosyl)-1-deoxynojirimycin (**69**) was also successfully synthesized via the same methodology from its corresponding disaccharide, and the precursor disaccharide for this transformation was synthesized via chemical glycosylation. Thus the methodology presented appears general and, though yields vary between the individual examples, glycosylated DNJ derivatives can be prepared without difficulties from their glycosylated glucose counterparts, as long as the latter are synthetically tractable.

Experimental Section

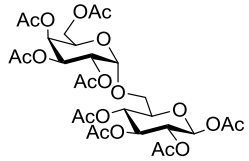
General methods: All solvents and reagents were obtained commercially and used as received unless stated otherwise. Reactions were executed at room temperature unless stated otherwise. Moisture sensitive reactions were performed under argon atmosphere. Water was removed from starting compounds by coevaporation 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 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.[19] 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) 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. Purification on HPLC were performed on a Prep LCMS, Gemini from Phenomenex B.V. (C-18, 110 Å, 5 μm, 19 x 150 mm column).

***Figure 7**: Proton and carbon NMR numbering of iminosugars:*



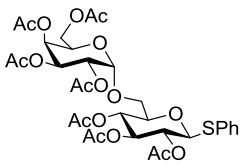
Synthesis of 6-*O*-(α-D-galactopyranosyl)-1-deoxynojirimycin (24)

1,2,3,4-Tetra-*O*-acetyl-6-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl)-β-glucopyranose (17):



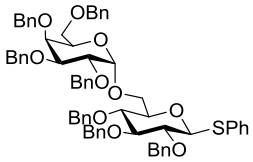
A suspension of Ac_2O (59.0 mL, 0.625 mol) and NaOAc (4.21 g, 51.3 mmol) were heated to reflux. When refluxing began the heat source was removed and melibiose (10.0 g, 29.2 mmol), which was co-evaporated with toluene (3 x), was added in small portions. The mixture was heated to reflux for 1 hour. TLC analysis confirmed complete consumption of the starting material **16** (1:1, PE:EtOAc, R_F = 0.39). The mixture was poured into ice water (400 mL) which was vigorously stirred. DCM (150 mL) was added and the layers were separated. The organic layer was washed with cold water (150 mL), sat. aq. $NaHCO_3$ solution (2 x 150 mL) and brine (150 mL). After the organic layer was dried (Na_2SO_4), filtered, and concentrated. The residue was purified with silica gel column chromatography (2:1 → 1:1 → 1:2, PE:EtOAc) to give **17** in 90% yield (17.8 g, 26.2 mmol). R_F = 0.39 (1:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.70 (d, *J* = 8.3 Hz, 1H, H-1), 5.45 (d, *J* = 2.9 Hz, 1H, H-4'), 5.34 (dd, *J* = 10.8, 3.3 Hz, 1H, H-3'), 5.27 (t, *J* = 9.4 Hz, 1H, H-4), 5.16 (m, 1H, H-1), 5.07 (m, 2H, H-2, H-3), 4.21 (dd, *J* = 11.4, 5.0 Hz, 1H, H-5'), 4.15 – 4.02 (m, 3H, H-2', H_2-6), 3.83 (ddd, *J* = 9.9, 3.9, 2.6 Hz, 1H, H-5), 3.74 (dd, *J* = 11.7, 4.3 Hz, 1H, H-6'a), 3.65 (dd, *J* = 11.8, 2.3 Hz, 1H, H-6'b), 2.24 – 1.96 (m, 24H, 8 x CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7 – 169.1 (C=O), 96.5 (C-1'), 91.7 (C-1), 73.6 (C-5), 70.3 (C-3), 68.4 (C-4), 68.2 (C-4'), 68.1 (C-2), 67.6 (C-3'), 66.6 (C-5'), 65.8 (C-6), 61.9 (C-6'), 20.9 – 20.7 (8 x CH_3).

2,3,4-Tri-*O*-acetyl-6-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl)-1-thio-D-glucopyranose (18):



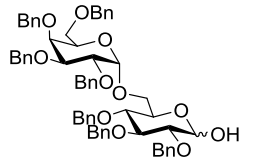
PhSH (5.2 mL, 51.0 mmol) was added to a stirred solution of **17** (17.8 g, 26.2 mmol) in dry DCM (50 mL) and kept under argon atmosphere. After cooling the solution (0 °C), $BF_3{\cdot}Et_2O$ (4.9 mL, 39.7 mmol) was added dropwise, turning the solution to orange. The mixture was stirred for 4 hours at r.t., after which TLC analysis showed complete consumption of the starting material. DCM (50 mL) was added to the reaction mixture and the solution was washed with sat. aq. $NaHCO_3$ solution (100 mL, 2 x). The organic layer was dried (Na_2SO_4). After filtering, concentrating and evaporating of the volatiles, the crude product was purified with silica gel column chromatography (3:1 → 7:3 → 5:3 → 1:1, PE:EtOAc), to give **18** as a pure white solid product in 82% yield (15.6 g, 21.4 mmol), R_F = 0.43 (1:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (dd, *J* = 8.0, 1.4 Hz, 2H, H_{Ar} SPh), 7.40 – 7.30 (m, 3H, H_{Ar} SPh), 5.35 (dd, *J* = 3.5, 1.2 Hz, 1H, H-4'), 5.32 (dd, *J* = 10.2, 3.4 Hz, 1H, H-3'), 5.24 (t, *J* = 9.4 Hz, 1H, H-3), 5.14 (d, *J* = 3.7 Hz, 1H, H-1'), 5.11 (dd, *J* = 10.2, 3.7 Hz, 1H, H-2'), 5.03 (t, *J* = 9.6 Hz, 1H, H-4), 4.96 (dd, *J* = 10.1, 9.2 Hz, 1H, H-2), 4.78 (d, *J* = 10.1 Hz, 1H, H-1), 4.21 (td, *J* = 6.6, 1.3 Hz, 1H, H-5'), 4.03 (d, *J* = 6.9 Hz, 2H, H_2-6'), 3.77 (dd, *J* = 10.6, 5.8 Hz, 1H, H-6b), 3.71 (dd, *J* = 5.8, 2.0 Hz, 1H, H-5), 3.56 (dd, *J* = 10.7, 1.9 Hz, 1H, H-6a), 2.15 – 1.99 (m, 21H, 7 x CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6 – 169.4 (C=O), 132.2 (C_{Ar} Ph), 132.1 (C_q SPh), 129.3, 128.4 (C_{Ar} SPh), 96.4 (C-1'), 85.7 (C-1), 76.8 (C-5), 74.1 (C-3), 70.1 (C-2), 68.8 (C-4), 68.2 (C-2'), 68.2 (C-4'), 67.5 (C-3'), 66.9 (C-6), 66.6 (C-5'), 61.8 (C-6'), 21.0 – 20.7 (7 x CH_3). $[\alpha]^{20}_D$ = +73.3 (c = 1.14, $CHCl_3$). IR/cm^{-1}: 1750, 1734, 1373, 1218, 1037.

2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-1-thio-D-glucopyranose (20):



18 (15.0 g, 20.6 mmol) was co-evaporated with toluene (3 x), after which it was dissolved in dry MeOH (100 mL). A catalytic amount of NaOMe was added and the reaction mixture was stirred for two hours. TLC-MS analysis showed complete conversion of the starting material into a polar product. The mixture was diluted with MeOH after which amberlite H^+ was added until pH was adjusted to 7. After filtering and concentrating the deprotected sugar (**19**) was co-evaporated with toluene (3 x). **19** was dissolved in DMF (100 mL), BnBr (20.9 mL, 176 mmol) was added, the solution was cooled (0 °C). NaH (14.5 g, 360 mmol) was added in small portions, after which the solution was stirred overnight under argon atmosphere. TLC analysis showed complete consumption of the starting compound (1:1, PE:EtOAc). After cooled down to 0 °C, the reaction mixture was sequently quenched by the addition of MeOH, the volatiles evaporated and EtOAc (200 mL) was added. The mixture was washed with HCl solution (1M, 100 mL, 2 x). After being dried (Na_2SO_4), filtered, and concentrated, the crude product was purified with silica gel column chromatography (17:3 → 4:1 → 1:1, PE:EtOAc) to give **20** in 50% yield over the 2 steps (11.0 g, 10.3 mmol). R_F = 0.88 (1:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.12 (m, 40H, H_{Ar} SPh/Bn), 5.03 (d, *J* = 3.5 Hz, 1H, H-1'), 4.66 (d, *J* = 9.9 Hz, 1H, H-1), 4.97 – 4.37 (m, 14H, 7 x CH_2 Bn), 4.05 (dd, *J* = 9.7, 3.5 Hz, 1H, H-2'), 3.99 (t, *J* = 6.5 Hz, 1H, H-5), 3.89 (m, 1H, H-3'), 3.86 (d, *J* = 2.9 Hz, 1H, H-4'), 3.78 (qd, *J* = 11.7, 3.5 Hz, 2H, H_2-6'), 3.68 – 3.59 (m, 2H, H-3, H-4), 3.54 (dd, *J* = 9.3, 5.9 Hz, 1H, H-5'), 3.49 (dd, *J* = 9.5, 6.5 Hz, 2H, H_2-6), 3.26 (dd, *J* = 9.9, 8.5 Hz, 1H, H-2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.0 – 138.1 (C_q Bn), 134.2 (C_q SPh), 131.9 – 127.5 (CH_{Ar} Bn), 97.9 (C-1'), 87.8 (C-1), 86.8 (C-3), 81.2 (C-2), 79.0 (C-5), 78.5 (C-4'), 78.0 (C-4), 76.9 (C-2), 75.8, 75.6 (2 x CH_2 Bn), 75.3 (C-3'), 75.1, 74.9, 73.4, 73.2, 72.8 (5 x CH_2 Bn), 72.8, 69.3 (C-5), 69.1 (C-6), 66.4 (C-6'). IR/cm^{-1}: 3088, 3063, 3030, 2905, 2866, 1454, 1352, 1094, 1040.

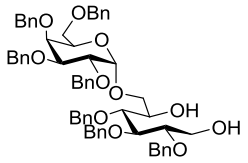
2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-α/β-glucopyranose (21):



NIS (22 mg, 97 µmol) and 30 µL of TFA were added to a cooled solution of **20** (94 mg, 88 µmol) in 2 mL DCM at 0 °C. After an hour of stirring TLC, analysis (4:1, toluene:EtOAc) showed complete consumption of the starting material. Sat. aq. $Na_2S_2O_3$ solution (7 mL) followed by sat. aq. $NaHCO_3$ solution (7 mL) was added. The mixture was diluted with DCM, after 30 minutes of stirring the layers were separated. The organic layer was dried ($MgSO_4$) and after filtering and concentrating the crude product was purified on silica gel column chromatography (9:1 → 7:3 → 6:4, PE:EtOAc) to give **21** in 77% yield (70 mg, 68 µmol). R_F = 0.30 and 0.40 (7:3, PE:EtOAc). For the major anomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.19 (m, 35H, H_{Ar} Bn), 5.09 (d, *J* = 3.6 Hz, 1H, H-1'), 4.98 (d, *J* = 3.5 Hz, 1H, H-1), 4.95 – 4.28 (m, 14H, 7 x CH_2 Bn), 4.13 (dt, *J* = 14.3, 6.8 Hz, 1H, H-5'), 4.07 – 3.98 (m, 2H, H-4, H-5), 3.96 – 3.88 (m, 3H, H-2', H-3, H-4'), 3.85 (d, *J* = 11.7 Hz, 1H, H-6'a), 3.72 (dd, *J* = 12.0, 5.5 Hz, 1H, H-6'b), 3.64 – 3.43 (m, 3H, H-2, H_2-6), 3.39 (dd, *J* = 9.4, 3.5 Hz, 1H, H-2), 3.26 (dd, *J* = 8.6, 7.3 Hz, 1H, H-3'). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 138.8, 138.4, 138.3, 138.1, 137.9, 137.8 (7 x C_q Bn), 128.6 – 127.6 (CH_{Ar} Bn), 98.5 (C-1'), 91.1 (C-1), 83.6 (C-3'), 81.9 (C-3), 80.4 (C-4), 78.6 (C-2), 78.2 (C-2'), 76.7 (C-4'), 75.8 – 72.7 (7 x CH_2 Bn), 70.8 (C-5'), 69.6 (C-5), 69.6 (C-6), 67.8 (C-6'). $[\alpha]^{20}_D$ = +38.1 (c = 1.03, $CHCl_3$). IR/cm^{-1}: 3030, 2920, 2868, 2247, 1497, 1454, 1357, 1090, 1026. HRMS: found 995.43431 $[C_{61}H_{64}O_{11}+Na]^+$, calculated for $[C_{61}H_{64}O_{11}+Na]^+$ 995.43408.

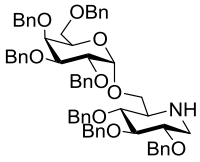
2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-D-glucitol (22):

$LiAlH_4$ in THF (6.0 mL, 2 M, 12.0 mmol) was slowly added to a cooled (0 °C) solution of **21** (3.91 g, 4.02 mmol, co-evaporated 3 x with toluene), in dry THF (40 mL) under argon atmosphere.



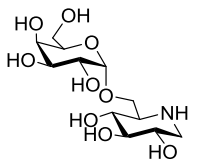
The mixture was stirred overnight allowing the temperature to reach r.t. TLC analysis showed absent of the starting compound (7:3, PE:EtOAc). The mixture was cooled in an ice-bath, after which it was slowly quenched by addition of H_2O. Then NaOH solution (3M, 40 mL) was added followed by Celite. The solution was stirred until a homogenous mixture was formed and after which it was filtered and the filter cake rinsed with Et_2O. H_2O (50 mL) and EtOAc (50 mL) was added and the organic layer was dried (Na_2SO_4), filtered and concentrated, the residue was purified with silica gel column chromatography (4:1 → 7:3 → 3:2, PE:EtOAc) to give **22** as an yellow oil in 74% yield (2.88 g, 2.95 mmol). R_F = 0.22 (7:3, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.19 (m, 35H, H_{Ar} Bn), 4.88 (d, *J* = 3.7 Hz, 1H, H-1'), 5.03 – 4.29 (m, 14H, 7 x CH_2 Bn), 4.06 (dd, *J* = 10.0, 3.6 Hz, 1H, H-2'), 4.02 – 3.93 (m, 3H, H-4', H-5, H-5'), 3.92 – 3.86 (m, 2H, H-3, H-3'), 3.82 (dd, *J* = 11.1, 5.3 Hz, 1H, H-6a), 3.73 (ddd, *J* = 20.7, 12.0, 4.8 Hz, 4H, H-4, H-1a, H-2, H-4', H-6b), 3.55 (dd, *J* = 11.3, 4.3 Hz, 1H, H-1b), 3.49 (d, *J* = 6.5 Hz, 2H, H_2-6'). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7 – 138.0 (C_q Bn), 128.6-127.5 (CH_{Ar} Bn), 99.0 (C-1'), 79.6 (C-3), 79.4 (C-4), 79.2 (C-2), 78.5 (C-3'), 76.5 (C-2'), 74.9, 74.9 (2 x CH_2 Bn), 74.8 (C-4'), 73.9 – 72.9 (5 x CH_2 Bn), 70.6 (C-6), 70.4 (C-5'), 69.8 (C-5), 69.0 (C-6'), 61.9 (C-1). $[\alpha]^{20}_D$ = +34.4 (c = 1.02, $CHCl_3$). IR/cm^{-1}: 3335, 2974, 2289, 1636, 1456, 1418, 1088, 1045. HRMS: found 997.44913 $[C_{61}H_{64}O_{11}+Na]^+$, calculated for $[C_{61}H_{64}O_{11}+Na]^+$ 997.44973.

2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-α-D-galactopyranosyl)-1-deoxynojirimycin (23):



A solution of $(COCl)_2$ (1.2 mL, 14.0 mmol) in dry DCM (15 mL) under argon atmosphere, was cooled to -78 °C. DMSO (1.2 mL, 16.9 mmol) dissolved in dry DCM (12 mL) was added dropwise. After 40 minutes **22** (4.28 g, 3.22 mmol), which was co-evaporated with toluene (3 x), in dry DCM (18 mL), was added dropwise to the mixture. The reaction was stirred for 2 hours at -70 °C, after which Et_3N (5.4 mL, 38.7 mmol) was added dropwise. The mixture was gradually warmed to -5 °C after which it was poured into a cooled (0 °C) MeOH solution (200 mL) containing $NaCNBH_3$ (0.813 g, 12.3 mmol), $HCOONH_4$ (4.07 g, 64.5 mmol), and Na_2SO_4 (1.37 g, 9.67 mmol). The mixture was stirred overnight allowing the reaction to reach r.t. TLC analysis showed the formation of the product. After filtering, the solvents were evaporated, after which the residue was dissolved in EtOAc (200 mL). The solution was washed with sat. aq. $NaHCO_3$ solution (200 mL). The organic layer was dried (Na_2SO_4), filtered and concentrated, the crude product was purified with silica gel column chromatography (4:1 → 7:3 → 3:2 → 1:1, PE:EtOAc) to give the **23** in 71% yield (2.17 g, 2.27 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.16 (m, 35H, H_{Ar} Bn), 4.91 (d, *J* = 3.7 Hz, 1H, H-1'), 5.05 – 4.26 (m, 14H, 7 x CH_2 Bn), 4.06 (dd, *J* = 10.0, 3.6 Hz, 1H H-2'), 3.97 (d, *J* = 2.7 Hz, 1H, H-4'), 3.94 – 3.87 (m, 2H, H-3', H-5'), 3.86 (dd, *J* = 10.5, 5.3 Hz, 1H, H-6a), 3.64 (dd, *J* = 10.5, 2.6 Hz, 1H, H-6b), 3.54 (dd, *J* = 9.1, 2.5 Hz, 1H, H-6'a), 3.53 (t, *J* = 9.0 Hz, 1H, H-3), 3.49 (dd, *J* = 9.3, 6.1 Hz, 1H, H-6'b), 3.32 (t, *J* = 9.2 Hz, 1H, H-2), 3.31 (t, *J* = 9.5, 1H, H-4), 2.95 (dd, *J* = 12.5, 5.1, 1H, H-1'a), 2.68 (ddd, *J* = 9.6, 5.2, 2.6, 1H, H-5), 2.37 (dd, *J* = 12.4, 10.7, 1H, H-1'b). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.8 – 137.9 (C_q Bn), 128.4 – 127.4 (CH_{Ar} Bn), 99.0 (C-1'), 87.2 (C-3), 80.9 (C-4), 80.0 (C-2), 78.8 (C-3'), 76.8 (C-2'), 75.6, 75.1, 74.7 (3 x CH_2 Bn), 74.7 (C-4'), 73.6, 73.4, 72.6, 72.6 (4 x CH_2 Bn), 69.6 (C-5'), 69.4 (C-6), 68.8 (C-6'), 59.5 (C-5), 47.7 (C-1). IR/cm^{-1}: 3032, 2899, 2872, 1497, 1453, 1354, 1208, 1093, 1059, 1027. $[\alpha]^{20}_D$ = +58.2 (c = 0.5, $CHCl_3$). HRMS: found 956.47363 $[C_{61}H_{66}NO_9+H]^+$, calculated for $[C_{61}H_{66}NO_9+H]^+$ 956.47321.

6-*O*-(α-D-Galactopyranosyl)-1-deoxynojirimycin (24):

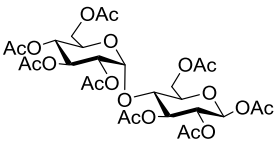


A mixture of DMF/MeOH (1:1, 20 mL), HCl (2 mL, 1M) and **23** (2.00 g, 2.09 mmol) was flushed with argon (3 x). Then a catalytic amount of Pd/C (20%) was added, after which H_2 was flushed through the mixture, and the solution shaken overnight under H_2 atmosphere (4 bar). HPLC analyses showed

complete conversion of starting material into the desired product. Then the catalyst was filtered and the solution was concentrated. The crude product was purified on size-exclusion column (NH_4HCO_3 in water 0.15 M). After co-evaporating (3 x) with Milli-Q water, product **24** was obtained as a white solid in 75% yield (326 mg, 1.00 mmol). ^{1}H NMR (400 MHz, MeOD) δ 4.84 (d, *J* = 3.4 Hz, 1H, H-1'), 4.01 (dd, *J* = 10.5, 4.7 Hz, 1H, H-6a), 3.90 (dd, *J* = 3.0, 1.2 Hz, 1H, H-4'), 3.84 (td, *J* = 6.1, 1.1 Hz, 1H, H-5'), 3.80 (dd, *J* = 10.1, 3.4 Hz, 1H, H-2'), 3.76 (dd, *J* = 10.1, 3.0 Hz, 1H, H-3'), 3.70 (d, *J* = 6.1 Hz, 2H, H_2-6'), 3.59 (dd, *J* = 10.4, 2.5 Hz, 1H, H-6b), 3.52 (ddd, *J* = 11.0, 9.1, 5.1 Hz, 1H, H-2), 3.38 (dd, *J* = 10.1, 9.0, 1H, H-4), 3.25 (t, *J* = 9.0 Hz, 1H, H-3), 3.20 (dd, *J* = 12.3, 5.1 Hz, 1H, H-1a), 2.82 (ddd, *J* = 10.0, 4.6, 2.6 Hz, 1H, H-5), 2.60 (dd, *J* = 12.3, 11.0 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, MeOD) δ 100.3 (C-1'), 79.9 (C-3), 72.4 (C-5'), 71.6 (C-4), 71.5 (C-2), 71.2 (C-3'), 70.9 (C-4'), 70.4 (C-2'), 66.8 (C-6), 62.6 (C-6'), 60.5 (C-5), 49.9 (C-1). $[\alpha]^{20}_D$ = +92.8 (c = 1.0, MeOH). IR/cm^{-1}: 3482, 2928, 2962, 1653, 1506, 1409, 1437, 1387, 1255, 1092, 1063. HRMS: found 326.14465 $[C_{12}H_{23}NO_9+H]^+$, calculated for $[C_{12}H_{23}NO_9+H]^+$ 326.14456.

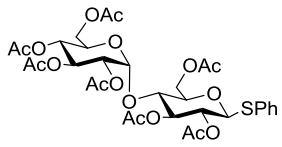
Synthesis of 4-*O*-α-D-glucopyranosyl-1-deoxynojirimycin (33)

1,2,3,6-Tetra-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-β-glucopyranose (26):



A suspension of Ac_2O (59.0 mL, 0.625 mol) and NaOAc (4.33 g, 52.8 mmol) was heated to reflux in an oil bath. When refluxing began the heat source was removed and maltose (9.94 g, 29.0 mmol, co-evaporated with toluene 3 x) was added in small portions. The mixture was heated again to reflux and after an hour, TLC analysis confirmed the formation of the product (1:1, PE:EtOAc, R_F = 0.36). The mixture was poured into ice water (400 mL) which was vigorously stirred. DCM (150 mL) was added and the layers were separated after which the organic layer was washed with water (200 mL), sat. aq. $NaHCO_3$ solution (2 x 150 mL) and brine (200 mL). After the organic layer was dried (Na_2SO_4), filtered, and concentrated, the residue was purified with silica gel column chromatography (1:1 → 1:2 → 0:1, PE:EtOAc) to give the pure **26** in 94% yield (18.5 g, 27.3 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.74 (d, *J* = 8.2 Hz, 1H, H-1), 5.42 (dd, *J* = 12.4, 4.0 Hz, 1H, H-1'), 5.36 (dd, *J* = 9.8, 2.3 Hz, 1H, H-3), 5.33 – 5.26 (m, 1H, H-3'), 5.11 – 4.94 (m, 2H, H-4', H-2), 4.86 (ddd, *J* = 10.5, 6.2, 4.0 Hz, 1H, H-2'), 4.45 (dd, *J* = 12.3, 2.4 Hz, 1H, H-6'a), 4.27 – 4.19 (m, 2H, H-6a, H-6'b), 4.14 – 4.08 (m, 1H, H-6b), 4.04 (ddd, *J* = 8.9, 5.8, 3.8 Hz, 1H, H-4), 3.96 – 3.91 (m, 1H, H-5'), 3.84 (ddd, *J* = 9.6, 4.3, 2.5 Hz, 1H, H-5), 2.26 – 1.96 (m, 24H, 8 x CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6 – 168.9 (8 x C=O), 95.8 (C-1'), 91.3 (C-1), 75.3 (C-3'), 73.0 (C-5), 72.4 (C-4), 71.0 (C-2), 70.1 (C-2'), 69.3 (C-3), 68.6 (C-5'), 68.0 (C-4'), 62.6 (C-6'), 61.5 (C-6), 20.9 – 20.6 (8 x CH_3).

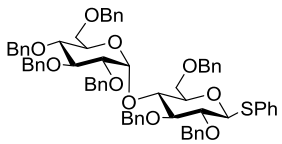
2,3,6-Tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-1-thio-D-glucopyranose (27):



27 was synthesised from **26** (18.5 g, 27.3 mmol) according to the procedure described for the preparation for compound **18**, to gain **27** (12.1 g, 16.5 mmol, 61% yield) as a colourless oil. R_F = 0.43 (1:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.44 (m, 2H, H_{Ar} SPh), 7.36 – 7.28 (m, 3H, H_{Ar} SPh), 5.39 (d, *J* = 4.0 Hz, 1H, H-1'), 5.34 (dd, *J* = 10.5, 9.6 Hz, 1H, H-3), 5.28 (t, *J* = 8.9 Hz, 1H, H-3'), 5.04 (t, *J* = 9.9 Hz, 1H, H-4'), 4.85 (dd, *J* = 10.5, 4.0 Hz, 1H, H-2'), 4.79 (d, *J* = 9.0 Hz, 1H, H-2), 4.73 (d, *J* = 10.1 Hz, 1H, H-1), 4.54 (dd, *J* = 12.1, 2.5 Hz, 1H, H-6'a), 4.24 (dd, *J* = 10.5, 4.5 Hz, 1H, H-6a), 4.21 (dd, *J* = 10.2, 4.4 Hz, 1H, H-6'b), 4.04 (dd, *J* = 10.2, 4.4 Hz, 1H, H-6b), 3.95 (dd, *J* = 9.7, 9.0 Hz, 1H, H-4), 3.94 (ddd, *J* = 10.4, 4.0, 2.4 Hz, 1H, H-5'), 3.72 (ddd, *J* = 9.8, 4.8, 2.6 Hz, 1H, H-5), 2.14 – 1.99 (m, 21H, 7 x CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7 – 169.6 (C=O), 133.5 (C_{Ar} SPh), 131.4 (C_q SPh), 129.0, 128.6 (C_{Ar} SPh), 95.7 (C-1'), 85.2 (C-1), 76.6 (C-3'), 76.2 (C-5), 72.5 (C-4), 70.8 (C-2), 70.1 (C-2'), 69.4 (C-3), 68.6

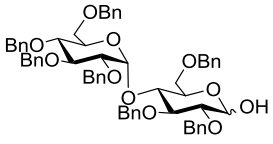
(C-5'), 68.1 (C-4'), 62.9 (C-6'), 61.6 (C-6), 21.1 – 20.7 (CH_3). $[\alpha]^{20}_D$ = +30.6 (c = 1.0, $CHCl_3$). IR/cm^{-1}: 1746, 1368, 1223, 1038, 912.

2,3,6-Tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-1-thio-D-glucopyranose (29):



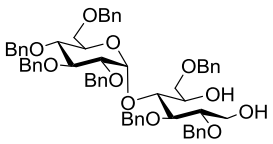
29 was synthesised from **27** (11.9 g, 13.3 mmol) according to the procedure described for the preparation for compound **19**, to gain **29** (15.4 g, 14.5 mmol, 89% yield) as a light yellow oil. R_F = 0.63 (4:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 6.5, 3.0 Hz, 2H, H_{Ar} SPh), 7.33 – 7.16 (m, 32H, H_{Ar} Bn, H_{Ar} SPh), 7.13 – 7.08 (m, 6H, H_{Ar} Bn), 5.64 (d, *J* = 3.6 Hz, 1H, H-1'), 4.92 – 4.76 (m, 6H, 3 x CH_2 Bn), 4.70 (d, *J* = 9.7 Hz, 1H, H-1), 4.62 – 4.41 (m, 7H, 7 x CH*H* Bn), 4.31 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 4.12 (t, *J* = 9.2 Hz, 1H, H-4), 3.93 (dd, *J* = 9.9, 8.9 Hz, 1H, H-3'), 3.89 (dd, *J* = 11.3, 4.3 Hz, 1H, H-6'a), 3.83 (dd, *J* = 6.5, 4.3 Hz, 1H, H-6'b), 3.82 (t, *J* = 8.8 Hz, 1H, H-3), 3.79 (dd, *J* = 7.3, 2.7 Hz, 1H, H-5'), 3.67 (dd, *J* = 17.1, 8.0 Hz, 1H, H-4'), 3.60 (dd, *J* = 11.2, 1.8 Hz, 1H, H-6a), 3.59 (dd, *J* = 10.5, 3.3 Hz, 1H, H-5), 3.58 (t, *J* = 10.2 Hz, 1H, H-2), 3.51 (dd, *J* = 9.9, 3.7 Hz, 1H, H-2'), 3.45 (dd, *J* = 10.6, 1.8 Hz, 1H, H-6b). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7 – 137.8 (7 x C_q Bn), 133.7 (C_q SPh), 132.0 – 126.5 (C_{Ar} SPh), 97.1 (C-1'), 87.2 (C-1), 86.7 (C-3), 82.0 (C-3'), 80.9 (C-2), 79.4 (C-2'), 78.8 (C-5), 77.7 (C-4'), 75.5 – 73.3 (7 x CH_2Bn), 72.7 (C-4), 71.1 (C-5'), 69.2 (C-6'), 68.3 (C-6). $[\alpha]^{20}_D$ = + 2.87 (c = 2.31, $CHCl_3$). IR/cm^{-1}: 3063, 3030, 2904, 2864, 1452, 1360, 1207, 1140, 1084, 1055, 1026.

2,3,6-Tri-O-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-α/β-glucopyranose (30):



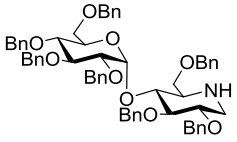
30 was synthesised from **29** (14.5 g, 13.6 mmol) according to the procedure described for the preparation for compound **21**, to gain **30** (12.3 g, 12.3 mmol, 93% yield) as a light yellow oil. R_F = 0.40 and 0.30 (7:3, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.07 (m, 35H, H_{Ar} Bn), 5.66 (dd, *J* = 8.6, 3.6 Hz, 1H, H-1'), 5.21 (t, *J* = 2.9 Hz, 1H, H-1), 5.02 – 4.26 (m, 14H, 7 x CH_2 Bn), 4.31 (dd, *J* = 12.2, 10.0 Hz, 1H, H-4), 4.13 (t, *J* = 8.8 Hz, 1H, H-3), 4.03 – 3.82 (m, 2H, H-3', H-5), 3.80 – 3.58 (m, 5H, H-2, H-4', H-5', H_2-6'), 3.55 – 3.45 (m, 2H, H-2', H-6a), 3.39 (ddd, *J* = 10.7, 3.6, 1.7 Hz, 1H, H-6b). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 138.7, 138.4, 138.2, 138.0, 137.9, 137.7 (7 x C_q Bn), 128.4 – 127.1 (CH_{Ar} Bn), 96.9 (C-1'), 90.7 (C-1), 82.0 (C-3'), 81.4 (C-4), 80.0 (C-2), 79.4 (C-2'), 77.7 (C-4'), 75.6 – 72.9 (7 x CH_2 Bn), 72.9 (C-3), 71.1 (C-5), 69.6 (C-5'), 69.2 (C-6'), 68.1 (C-6). $[\alpha]^{20}_D$ = +32.8 (c = 1.0, $CHCl_3$). IR/cm^{-1}: 3418, 3063, 3030, 2903, 2864, 1497, 1452, 1362, 1265, 1207, 1146, 1088, 1043, 1026.

2,3,6-Tri-O-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-D-glucitol (31):



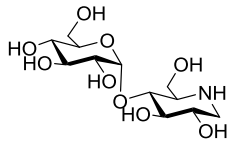
31 was synthesised from **30** (11.3 g, 11.6 mmol) according to the procedure described for the preparation for compound **22**, to gain **31** (8.33 g, 8.55 mmol, 74% yield) as a light yellow oil. R_F = 0.31 (7:3, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.07 (m, 35H, H_{Ar} Bn), 4.82 (d, *J* = 3.1 Hz, 1H, H-1'), 4.96 – 4.35 (m, 14H, 7 x CH_2 Bn), 4.12 (dd, *J* = 8.6, 4.0 Hz, 1H, H-3'), 3.98 (ddd, *J* = 10.2, 3.2, 2.1 Hz, 1H, H-5), 3.96 – 3.90 (m, 4H, H-5', H-4, H-3', H-4'), 3.71 (dt, *J* = 29.8, 6.9 Hz, 2H, H-1), 3.60 – 3.53 (m, 6H, H_2-6, H_2-6', H-2, H-2'). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2 – 137.6 (C_q Bn), 129.1 – 125.4 (CH_{Ar} Bn), 99.2 (C-1'), 82.0 (C-3), 79.9 (C-3'), 79.7 (C-4'), 79.4 (C-2), 78.8 (C-4), 77.8 (C-2'), 75.7 – 72.8 (7 x CH_2 Bn), 71.8 (C-3'), 71.6 (C-6), 71.2 (C-5), 68.3 (C-6'), 61.6 (C-1). $[\alpha]^{20}_D$ = +38.1 (c = 1.03, $CHCl_3$). IR/cm^{-1}: 3420, 3063, 3030, 2862, 1454, 1207, 1086, 1070, 1028. HRMS: found 997.44970 $[C_{61}H_{64}O_{11}+Na]^+$, calculated for $[C_{61}H_{64}O_{11}+Na]^+$ 997.44973.

2,3,6-Tri-O-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-1-deoxynojirimycin (32):



32 was synthesised from **31** (0.998 g, 1.02 mmol) according to the procedure described for the preparation for compound **23**, to gain **32** (0.428 g, 0.448 mmol, 44% yield) as a light yellow oil. R_F = 0.38 (1:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.26 (m, 35H, H_{Ar} Bn), 5.94 (d, *J* = 3.6 Hz, 1H, H-1'), 5.30 – 4.46 (m, 14H, CH_2 Bn), 4.11 (dd, *J* = 9.8, 8.5 Hz, 1H, H-3'), 3.98 (dd, *J* = 9.5, 8.7 Hz, 1H, H-4), 3.93 – 3.87 (m, 2H, H-5', H-6a), 3.88 (t, *J* = 8.7 Hz, 1H, H-3), 3.84 (dd, *J* = 8.7, 1.3 Hz, 1H, H-4'), 3.81 (dd, *J* = 8.7, 5.6 Hz, 1H, H-6b), 3.73 (dd, *J* = 10.6, 2.8 Hz, 1H, H-6'a), 3.73 – 3.70 (m, 1H, H-2), 3.67 (dd, *J* = 9.8, 3.6 Hz, 1H, H-2'), 3.61 (dd, *J* = 10.4, 1.3 Hz, 1H, H-6'b), 3.42 (dd, *J* = 12.3, 5.1 Hz, 1H, H-1a), 3.03 (ddd, *J* = 9.1, 5.8, 2.9, 1H, H-5), 2.70 (dd, *J* = 12.3, 10.6 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.1 – 137.9 (7 x C_q Bn), 128.3 – 126.5 (CH_{Ar} Bn), 96.6 (C-1'), 87.0 (C-3), 82.0 (C-3'), 80.9 (C-2), 79.3 (C-2'), 77.7 (C-4'), 75.5, 74.9 (2 x CH_2 Bn), 74.2 (C-4), 73.8 – 72.5 (5 x CH_2 Bn), 71.0 (C-5'), 70.5 (C-6), 68.1 (C-6'), 59.0 (C-5), 47.8 (C-1). $[\alpha]^{20}_D$ = +26.0 (c = 0.7, $CHCl_3$). IR/cm^{-1}: 2918, 2866, 1454, 1362, 1740, 1090, 1072, 1047, 1026. HRMS: found 956.47311 $[C_{61}H_{66}NO_9+H]^+$, calculated for $[C_{61}H_{66}NO_9+H]^+$ 956.47321.

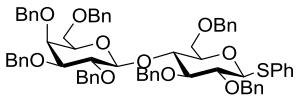
4-*O*-(α-D-Glucopyranosyl)-1-deoxynojirimycin (33):



33 was synthesised from **32** (1.00 g, 1.04 mmol) according to the procedure described for the preparation for compound **24**, to gain **33** (0.24 g, 0.74 mmol, 71% yield) as a light yellow oil. ^{1}H NMR (400 MHz, MeOD) δ 5.21 (d, *J* = 3.7 Hz, 1H, H-1'), 4.00 (dd, *J* = 12.1, 4.8 Hz, 1H, H-6a), 3.91 (dd, *J* = 12.0, 3.0 Hz, 1H, H-6b), 3.88 – 3.83 (m, 1H, H-6'a), 3.77 (ddd, *J* = 4.8, 8.9, 10.8 Hz, 1H, H-2). 3.81 – 3.66 (m, 4H, H-3', H-4', H-6'b, H-3), 3.62 (dd, *J* = 9.7, 9.0 Hz, 1H, H-4) 3.49 (dd, *J* = 9.7, 3.8 Hz, 1H, H-2'), 3.35 (dd, *J* = 12.5, 5.0 Hz, 1H, H-1a), 3.30 – 3.23 (m, 2H, H-5', H-5), 2.91 (dd, *J* = 12.4, 10.9 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, MeOD) δ 103.1 (C-1'), 79.3 (C-3'), 77.7 (C-3), 75.1 (C-4'), 74.9 (C-4), 73.9 (C-2'), 71.4 (C-5'), 68.2 (C-2), 62.7 (C-6'), 60.5 (C-5), 58.8 (C-6), 47.1 (C-1). $[\alpha]^{20}_D$ = +25.0 (c =0.2, MeOH). IR/cm^{-1}: 3303, 2967, 1636, 1560, 1203, 1161, 1022. HRMS: found 326.14464 $[C_{12}H_{23}NO_9+H]^+$, calculated for $[C_{12}H_{23}NO_9+H]^+$ 326.14456.

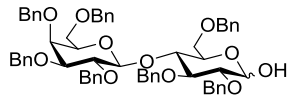
Synthesis of β-D-galactopyranosyl-1-deoxynojirimycin (40)

2,3,6-Tri-*O*-benzyl-4-(2',3',4',6'-tetra-*O*-benzyl-β-D-galactopyranosyl)-1-thio-D-glucopyranose (36):



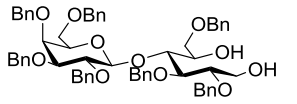
36 was synthesised from **34** (3.64 g, 5.00 mmol) according to the procedure described for the preparation for compound **20**, to gain **36** (5.32 g, 5.00 mmol, 100% yield) as a light yellow oil. R_F = 0.67 (4:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.04 (m, 40H, H_{Ar} Bn/SPh), 4.67 (d, *J* = 10.5 Hz, 1H, H-1), 5.13 – 4.20 (m, 14H, 7 x CH_2 Bn), 4.45 (d, *J* = 7.7 Hz, 1H, H-1'), 4.00 – 3.91 (m, 2H, H-4', H-5'), 3.82 (dd, *J* = 11.0, 4.3 Hz, 1H, H-6'a), 3.79 – 3.73 (m, 2H, H-2', H-6'b), 3.61 (t, *J* = 8.9 Hz, 1H, H-3'), 3.52 (t, *J* = 7.6 Hz, 1H, H-6a), 3.47 – 3.31 (m, 5H, H-2, H-3, H-4, H-5 H-6b). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.2 – 138.2 (7 x C_q Bn), 133.8 (C_q SPh), 132.2 – 127.3 (CH_{Ar} Bn/SPh), 103.0 (C-1'), 87.5 (C-1), 85.1 (C-3'), 82.7 (C-4), 80.2 (C-2), 80.1 (C-2'), 79.5 (C-3), 76.6 (C-4'), 75.7, 75.6, 75.5, 74.5 (4 x CH_2 Bn), 73.7 (C-5'), 73.5, 73.2 (2 x CH_2 Bn), 73.1 (C-5), 72.2 (CH_2 Bn), 68.5 (C-6'), 68.2 (C-6). IR/cm^{-1}: 3030, 2920, 2862, 1497, 1454, 1362, 1209, 1088, 1076, 1028, 1001.

2,3,6-Tri-*O*-benzyl-4-(2',3',4',6'-tetra-*O*-benzyl-β-D-galactopyranosyl)-α/β-D-glucopyranose (37):



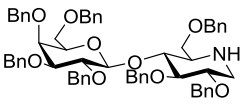
37 was synthesised from **36** (0.12 g, 0.12 mmol) according to the procedure described for the preparation for compound **21**, to gain **37** (96.0 mg, 98.7 µmol, 85% yield) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.04 (m, 40H, H_{Ar} Bn/SPh), 5.16 (d, *J* = 3.7 Hz, 1H, H-1), 5.10 – 4.17 (m, 14H, 7 x CH_2 Bn), 4.33 (d, *J* = 9.4 Hz, 1H, H-1'), 3.99 – 3.87 (m, 3H, H-2', H-3', H-5'), 3.87 – 3.80 (m, 2H, H-4, H-3), 3.74 (ddd, *J* = 10.0, 7.5, 2.4 Hz, 1H, H-6'a), 3.65 (dd, *J* = 10.5, 1.6 Hz, 1H, H-6'b), 3.52 (ddd, *J* = 12.7, 9.3, 6.7 Hz, 2H, H-2, H-6a), 3.42 – 3.29 (m, 4H, H-3, H-4', H-5, H-6b). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.3 – 138.1 (C_q Bn), 128.5 – 127.2 (CH_{Ar} Bn), 103.0 (C-1'), 91.5 (C-1), 82.5 (C-3), 80.0 (C-2), 79.2 (C-2'), 76.6 (C-3'), 75.5, 72.3 (2 x CH_2 Bn), 75.1 (C-4'), 74.8 (CH_2 Bn), 73.8 (C-4), 73.7, 73.6, 73.2 (3 x CH_2 Bn), 73.2 (C-5'), 72.7 (CH_2 Bn), 70.5 (C-5), 68.3 (C-6'), 68.1 (C-6). $[\alpha]^{20}_D$ = +12.4 (c = 1.07, $CHCl_3$). IR/cm^{-1}: 2920, 2864, 1452, 1396, 1362, 1207, 1090. HRMS: found 995.43425 $[C_{61}H_{64}O_{11}+Na]^+$, calculated for $[C_{61}H_{64}O_{11}+Na]^+$ 995.43408.

2,3,6-Tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-D-glucitol (38):



38 was synthesised from **37** (5.44 g, 5.59 mmol) according to the procedure described for the preparation for compound **22**, to gain **38** (4.17 g, 4.28 mmol, 77% yield) as a light yellow oil. R_F = 0.20 (7:3, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.18 (m, 35H, H_{Ar} Bn), 4.97 – 4.22 (m, 14H, 7 x CH_2 Bn), 4.34 (dd, *J* = 7.2, 5.4 Hz, 1H, H-1'), 4.03 (dd, *J* = 7.4, 2.4 Hz, 1H, H-4), 3.99 (dt, *J* = 7.9, 3.8 Hz, 2H, H-2, H-5'), 3.95 (dd, *J* = 7.8, 2.4 Hz, 1H, H-3), 3.83 (d, *J* = 2.9 Hz, 1H, H-4'), 3.77 (dd, *J* = 9.8, 7.7 Hz, 1H, H-2'), 3.71 (dd, *J* = 6.9, 3.7, 2H, H-1), 3.66 (dd, *J* = 9.9, 4.4 Hz, 1H, H-6'a), 3.55 (dd, *J* = 9.8, 3.0 Hz, 1H, H-6'b), 3.48 (dd, *J* = 6.3, 2.5 Hz, 2H, H_2-6), 3.42 (dd, *J* = 10.0, 6.4 Hz, 1H, H-5), 3.40 (dd, *J* = 9.7, 3.0 Hz, 1H, H-3'). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.8 – 137.7 (C_q Bn), 128.5 – 127.3 (CH_{Ar} Bn), 103.8 (C-1'), 82.42 (C-3'), 79.9 (C-4), 79.8 (C-2), 79.4 (C-2'), 77.5 (C-3), 75.4, 74.9, 74.7 (3 x CH_2 Bn), 73.8 (C-4'), 73.6, 73.3 (2 x CH_2 Bn), 73.3 (C-5), 73.2, 73.0 (2 x CH_2 Bn), 70.8 (C-5'), 70.8 (C-6'), 68.9 (C-6), 62.3 (C-1). IR/cm^{-1}: 3028, 2922, 2864, 1063, 1026, 1001. $[\alpha]^{20}_D$ = +6.6 (c = 1.0, $CHCl_3$). HRMS: found 997.44976 $[C_{61}H_{66}O_{11}+Na]^+$, calculated for $[C_{61}H_{66}O_{11}+Na]^+$ 997.44973.

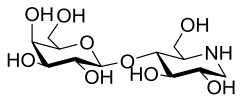
2,3,6-Tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-1-deoxynojirimycin (39):



39 was synthesised from **38** (4.17 g, 4.28 mmol) according to the procedure described for the preparation for compound **23**, to gain **39** (0.90 g, 0.94 mmol, 22% yield) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.09 (m, 35H, H_{Ar} Bn), 5.05 (d, *J* = 10.7 Hz, 1H, CH*H* Bn), 4.98 (d, *J* = 11.4 Hz, 1H), 4.85 (d, *J* = 11.4 Hz, 1H, CH*H* Bn), 4.83 (d, *J* = 2.6 Hz, 2H, CH_2 Bn), 4.75 (d, *J* = 11.9 Hz, 1H, CH*H* Bn), 4.71 (d, *J* = 11.6 Hz, 2H, CH_2 Bn), 4.67 (d, *J* = 11.5 Hz, 1H, CH*H* Bn), 4.57 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.44 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.38 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.35 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.34 (d, *J* = 7.7 Hz, 1H, H-1'), 4.30 (d, *J* = 11.9 Hz, 1H, CH*H* Bn), 3.92 (d, *J* = 3.0 Hz, 1H, H-4'), 3.78 (dd, *J* = 9.7, 7.7 Hz, 1H, H-2'), 3.70 (dd, *J* = 9.0, 2.8 Hz, 1H, H-6a), 3.65 (dd, *J* = 9.4, 6.1 Hz, 1H, H-6b), 3.57 (dd, *J* = 9.8, 5.0 Hz, 1H, H-2), 3.52 (dd, *J* = 14.3, 7.4 Hz, 1H, H-6'a), 3.46 – 3.41 (m, 3H, H-5', H-3, H-4). 3.42 (dd, *J* = 9.8, 2.9 Hz, 1H, H-3'), 3.35 (dd, *J* = 14.0, 7.3 Hz, 1H, H-6'b), 3.20 (dd, *J* = 12.2, 4.5 Hz, 1H, H-1a), 2.71 (ddd, *J* = 9.2, 5.6, 2.6 Hz, 1H, H-5), 2.50 (dd, *J* = 12.2, 10.0 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.8 – 137.7 (C_q Bn), 128.6 – 127.6 (CH_2 Bn), 103.9 (C-1'), 82.5 (C-4'), 80.0 (C-5'), 79.8 (C-2'), 79.4 (C-3'), 77.6 – 74.7 (3 x CH_2 Bn), 73.7 (C-3), 73.6 (CH_2 Bn), 73.3 (C-5), 73.3 – 72.9 (3 x CH_2 Bn), 70.8 (C-2), 70.8 (C-6), 68.9 (C-6'), 62.3 (C-1). IR/cm^{-1}: 3060, 3029, 2916, 2866, 1497, 1453, 1361, 1208, 1097,

1028. $[\alpha]^{20}_D$ = +14.0 (c = 0.4, $CHCl_3$). HRMS: found 956.47340 $[C_{61}H_{66}O_9N$ +Na$]^+$, calculated for $[C_{61}H_{66}O_9N$+H$]^+$ 956.47321.

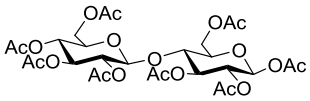
4-(β-D-Galactopyranosyl)-1-deoxynojirimycin (40):



40 was synthesised from **39** (0.932 g, 0.975 mmol) according to the procedure described for the preparation for compound **24**, to gain **40** (0.20 g, 0.621 mmol, 64% yield) as a light yellow oil. ^{1}H NMR (400 MHz, MeOD) δ 4.44 (d, *J* = 7.6 Hz, 1H, H-1'), 3.92 (d, *J* = 3.7 Hz, 2H, H_2-6), 3.92 (d, *J* = 3.2, Hz, 1H, H-4'), 3.87 (dd, *J* = 11.4, 7.4 Hz, 1H, H-6'a), 3.79 (dd, *J* = 11.4, 4.7 Hz, 1H, H-6'b), 3.67 (ddd, *J* = 7.4, 4.7, 1.1 Hz, 1H, H-5'), 3.65 (dd, *J* = 9.8, 7.6 Hz, 1H, H-2'), 3.58 (dd, *J* = 9.7, 3.3 Hz, 1H, H-3'), 3.55 (ddd, *J* = 10.7, 9.1, 5.1 Hz, 1H, H-2), 3.50 (dd, *J* = 9.5, 8.8 Hz, 1H, H-4), 3.44 (t, *J* = 8.7 Hz, 1H, H-3), 3.17 (dd, *J* = 12.4, 5.1 Hz, 1H, H-1a), 2.71 (dt, *J* = 9.6, 3.8 Hz, 1H, H-5), 2.54 (dd, *J* = 12.5, 10.7 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, MeOD) δ 106.1 (C-1'), 83.6 (C-4), 79.6 (C-3), 77.9 (C-5'), 75.7 (C-3'), 73.5 (C-2), 73.3 (C-2'), 71.1 (C-4'), 63.3 (C-6'), 62.8 (C-6), 62.5 (C-5), 51.3 (C-1). $[\alpha]^{20}_D$ = +16.0 (c = 0.2, MeOH). IR/cm^{-1}: 3306, 2945, 2833, 1653, 1448, 1410, 1113, 1018. HRMS: found 326.14482 $[C_{12}H_{23}NO_9$+H$]^+$, calculated for $[C_{12}H_{23}NO_9$+H$]^+$ 326.14456.

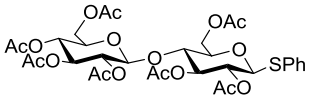
Synthesis of 4-*O*-(β-D-glucopyranosyl)-1-deoxynojirimycin (49)

2,3,6-Tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-1-thio-D-glucopyranose (42):



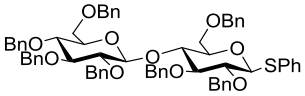
42 was synthesised from D-(+)-cellobiose (10.0 g, 29.2 mmol) according to the procedure described for the preparation for compound **17**, to gain **42** (19.5 g, 28.8 mmol, 98% yield). R_F = 0.36 (1:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.66 (d, *J* = 8.2 Hz, 1H, H-1), 5.23 (t, *J* = 9.2 Hz, 1H, H-3'), 5.18 – 4.99 (m, 3H, H-3, H-4, H-2), 4.97 – 4.87 (m, 1H, H-2'), 4.52 – 4.47 (m, 2H, H-6'a, H-1'), 4.37 (dd, *J* = 12.3, 4.4 Hz, 1H, H-6a), 4.12 (dd, *J* = 12.2, 4.6 Hz, 1H, H-6'b), 4.05 (dd, *J* = 12.5, 2.1 Hz, 1H, H-6b), 3.82 (dd, *J* = 15.6, 6.5 Hz, 1H, H-4'), 3.75 (ddd, *J* = 9.8, 4.7, 1.8 Hz, 1H, H-5), 3.66 (ddd, *J* = 9.9, 4.4, 2.4 Hz, 1H, H-5'). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6 – 169.0 (8 x C=O), 100.8 (C-1'), 91.7 (C-1), 76.0 (C-5'), 73.6 (C-4'), 73.0 (C-3'), 72.5 (C-3), 72.1 (C-5), 71.6 (C-2'), 70.5 (C-2), 67.9 (C-4), 61.7 (C-6'), 61.7 (C-6), 21.0 – 20.6 (8 x CH_3).

2,3,6-Tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-1-thio-D-glucopyranose (43):



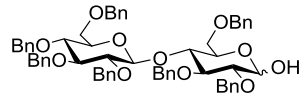
43 was synthesised from **42** (0.68 g, 1.00 mmol) according to the procedure described for the preparation for compound **18**, to gain **43** (0.67 g, 0.91 mmol, 91% yield) as a colourless oil. R_F = 0.53 (1:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.20 (dd, *J* = 10.4, 8.0 Hz, 1H, H-3'), 5.15 (dd, *J* = 9.4, 7.2 Hz, 1H, H-3), 5.06 (t, *J* = 9.7 Hz, 1H, H-4), 4.91 (ddd, *J* = 10.0, 8.6, 3.7 Hz, 2H, H-2, H-2'), 4.70 (d, *J* = 10.1 Hz, 1H, H-1'), 4.56 (dd, *J* = 11.9, 2.0 Hz, 1H, H-6'a), 4.54 (d, *J* = 7.9 Hz, 1H, H-1), 4.38 (dd, *J* = 12.5, 4.3 Hz, 1H, H-6a), 4.11 (td, *J* = 7.1, 1.9 Hz, 1H, H-6'b), 4.03 (dd, *J* = 12.4, 2.0 Hz, 1H, H-6b), 3.75 (m, 1H, H-4'), 3.69 (ddd, *J* = 8.9, 3.9, 1.8 Hz, 1H, H-5), 3.65 (dd, *J* = 5.7, 2.0 Hz, 1H, H-5'). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3 – 168.8 (7 x C=O), 132.8 (C_{Ar} SPh), 131.7 (C_q SPh), 128.7, 128.1 (C_{Ar} SPh), 100.5 (C-1'), 85.2 (C-1), 76.6 (C-5'), 76.2 (C-4'), 73.4 (C-3'), 72.8 (C-3), 71.7 (C-5), 71.4 (C-2'), 70.0 (C-2), 67.6 (C-4), 61.9 (C-6'), 61.4 (C-6), 20.9 – 20.3 (7 x CH_3). $[\alpha]^{20}_D$ = +30.6 (c = 1.0, $CHCl_3$). IR/cm^{-1}: 2958, 2872, 1743, 1440, 1368, 1216, 1168, 1038. HRMS: found 751.18783 $[C_{32}H_{40}O_{17}S$+Na$]^+$, calculated for $[C_{32}H_{40}O_{17}S$+Na$]^+$ 751.18784.

2,3,6-Tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-1-thio-D-glucopyranose (45):



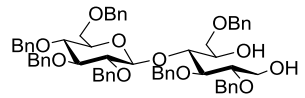
45 was synthesised from **43** (11.9 g, 13.3 mmol) according to the procedure described for the preparation for compound **19**, to gain **45** (15.4 g, 14.5 mmol, 89% yield) as a light yellow oil. R_F = 0.63 (4:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 6.5, 3.0 Hz, 2H, H_{Ar} SPh), 7.33 – 7.16 (m, 32H, H_{Ar} Bn, H_{Ar} SPh), 7.13 – 7.08 (m, 6H, H_{Ar} Bn), 5.64 (d, *J* = 3.6 Hz, 1H, H-1'), 4.92 – 4.76 (m, 6H, 3 x CH_2 Bn), 4.70 (d, *J* = 9.7 Hz, 1H, H-1), 4.62 – 4.41 (m, 7H, 7 x CH*H* Bn), 4.31 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 4.12 (t, *J* = 9.2 Hz, 1H, H-4), 3.93 (dd, *J* = 9.9, 8.9 Hz, 1H, H-3'), 3.89 (dd, *J* = 11.3, 4.3 Hz, 1H, H-6a'), 3.83 (dd, *J* = 6.5, 4.3 Hz, 1H, H-6b'), 3.82 (t, *J* = 8.8 Hz, 1H, H-3), 3.79 (dd, *J* = 7.3, 2.7 Hz, 1H, H-5'), 3.67 (dd, *J* = 17.1, 8.0 Hz, 1H, H-4'), 3.60 (dd, *J* = 11.2, 1.8 Hz, 1H, H-6a), 3.59 (dd, *J* = 10.5, 3.3 Hz, 1H, H-5), 3.58 (t, *J* = 10.2 Hz, 1H, H-2), 3.51 (dd, *J* = 9.9, 3.7 Hz, 1H, H-2'), 3.45 (dd, *J* = 10.6, 1.8 Hz, 1H, H-6b). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7 – 137.8 (7 x C_q Bn), 133.7 (C_q SPh), 132.0-126.5 (C_{Ar}), 97.1 (C-1'), 87.2 (C-1), 86.7 (C-3), 82.0 (C-3'), 80.9 (C-2), 79.4 (C-2'), 78.8 (C-5), 77.7 (C-4'), 75.5 – 73.3 (7 x CH_2Bn), 72.7 (C-4), 71.1 (C-5'), 69.2 (C-6'), 68.3 (C-6). $[\alpha]^{20}_D$ = + 2.87 (c = 2.31, $CHCl_3$). IR/cm^{-1}: 3063, 3030, 2904, 2864, 1452, 1360, 1207, 1140, 1084, 1055, 1026. HRMS: found 1087.44289 $[C_{61}H_{64}O_{11}+Na]^+$, calculated for $[C_{61}H_{64}O_{11}+Na]^+$ 1087.44254.

2,3,6-Tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-α/β-glucopyranose (46):



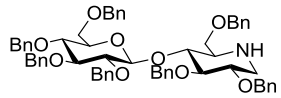
46 was synthesised from **45** (14.5 g, 13.6 mmol) according to the procedure described for the preparation for compound **21**, to gain **46** (12.3 g, 12.3 mmol, 90% yield) as a light yellow oil. R_F = 0.40 and 0.30 (7:3, PE:EtOAc). For the major anomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.07 (m, 35H, H_{Ar} Bn), 5.66 (dd, *J* = 8.6, 3.6 Hz, 1H, H-1'), 5.21 (t, *J* = 2.9 Hz, 1H, H-1), 5.02 – 4.26 (m, 14H, 7 x CH_2 Bn), 4.31 (dd, *J* = 12.2, 10.0 Hz, 1H, H-4), 4.13 (t, *J* = 8.8 Hz, 1H, H-3), 4.03 – 3.82 (m, 2H, H-3', H-5), 3.80 – 3.58 (m, 5H, H-2, H-4', H-5', H_2-6'), 3.55 – 3.45 (m, 2H, H-2', H-6a), 3.39 (ddd, *J* = 10.7, 3.6, 1.7 Hz, 1H, H-6b). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9 – 137.7 (7 x C_q Bn), 128.4 – 127.1 (CH_{Ar} Bn), 96.9 (C-1'), 90.7 (C-1), 82.0 (C-3'), 81.4 (C-4), 80.0 (C-2), 79.4 (C-2'), 77.7 (C-4'), 75.6 – 72.9 (7 x CH_2 Bn), 72.9 (C-3), 71.1 (C-5), 69.6 (C-5'), 69.2 (C-6'), 68.1 (C-6). $[\alpha]^{20}_D$ = +32.8 (c = 1.0, $CHCl_3$). IR/cm^{-1}: 3418, 3063, 3030, 2903, 2864, 1497, 1452, 1362, 1265, 1207, 1146, 1088, 1043, 1026. HRMS: found 995.43387 $[C_{61}H_{64}O_{11}+Na]^+$, calculated for $[C_{61}H_{64}O_{11}+Na]^+$ 995.43408.

2,3,6-Tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-D-glucitol (47):



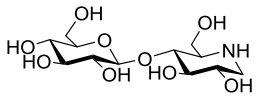
47 was synthesised from **46** (11.2 g, 11.6 mmol) according to the procedure described for the preparation for compound **22**, to gain **47** (8.33 g, 8.55 mmol, 74% yield) as a light yellow oil. R_F = 0.31 (7:3 PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.07 (m, 35H, H_{Ar} Bn), 4.82 (d, *J* = 3.1 Hz, 1H, H-1'), 4.96 – 4.35 (m, 14H, 7 x CH_2 Bn), 4.12 (dd, *J* = 8.6, 4.0 Hz, 1H, H-3'), 3.98 (ddd, *J* = 10.2, 3.2, 2.1 Hz, 1H, H-5), 3.96 – 3.90 (m, 4H, H-5', H-4, H-3', H-4'), 3.71 (dt, *J* = 29.8, 6.9 Hz, 2H, H_2-1), 3.52 – 3.62 (m, 6H, H_2-6, H_2-6', H-2, H-2'). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 138.2 – 137.6 (7 x C_q Bn), 129.1 – 125.4 (CH_{Ar} Bn), 99.2 (C-1'), 82.0 (C-3), 79.9 (C-3'), 79.7 (C-4'), 79.4 (C-2), 78.8 (C-4), 77.8 (C-2'), 75.7 – 72.8 (7 x CH_2 Bn), 71.8 (C-3'), 71.6 (C-6), 71.2 (C-5), 68.3 (C-6'), 61.6 (C-1). IR/cm^{-1}: 3420, 3063, 3030, 2862, 1454, 1207, 1086, 1070, 1028. $[\alpha]^{20}_D$ = +38.1 (c = 1.03, $CHCl_3$). HRMS: found 997.44972 $[C_{61}H_{66}O_{11}+Na]^+$, calculated for $[C_{61}H_{66}O_{11}+Na]^+$ 997.44973.

2,3,6-Tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)-1-deoxynojirimycin (48):



48 was synthesised from **47** (1.0 g, 1.02 mmo) according to the procedure described for the preparation for compound **23**, to gain **48** (0.43 g, 0.45 mmol, 44% yield) as a light yellow oil. R_F = 0.38 (1:1 PE, EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.26 (m, 35H, H_{Ar} Bn), 5.94 (d, *J* = 3.6 Hz, 1H, H-1'), 5.30 – 4.46 (m, 14H, 7 x CH_2 Bn), 4.11 (dd, *J* = 9.8, 8.5 Hz, 1H, H-3'), 3.98 (dd, *J* = 9.6, 8.7 Hz, 1H, H-4), 3.93 – 3.87 (m, 3H, H-5', H-6a, H-3), 3.84 (dd, *J* = 8.7, 1.3 Hz, 1H, H-4'), 3.81 (dd, *J* = 8.7, 5.6 Hz, 1H, H-6b), 3.73 (dd, *J* = 10.6, 2.8 Hz, 1H, H-6a'), 3.72 (td, *J* = 5.3, 2.2 Hz, 1H, H-2), 3.67 (dd, *J* = 9.8, 3.6 Hz, 1H, H-2'), 3.61 (dd, *J* = 10.4, 1.3 Hz, 1H, H-6b'), 3.42 (dd, *J* = 12.3, 5.1 Hz, 1H, H-1a), 3.03 (ddd, *J* = 9.0, 5.7, 2.8, 1H, H-5), 2.70 (dd, *J* = 12.3, 10.6 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.1 – 137.9 (7 x C_q Bn), 128.3 – 126.5 (CH_{Ar} Bn), 96.6 (C-1'), 87.0 (C-3), 82.0 (C-3'), 80.9 (C-2), 79.3 (C-2'), 77.7 (C-4'), 75.5, 74.9 (2 x CH_2 Bn), 74.2 (C-4), 73.8 – 72.5 (5 x CH_2 Bn), 71.0 (C-5'), 70.5 (C-6), 68.1 (C-6'), 59.0 (C-5), 47.8 (C-1). $[\alpha]^{20}_D$ = +26.0 (c = 0.7, $CHCl_3$). IR/cm^{-1}: 2918, 2866, 1454, 1362, 1740, 1090, 1072, 1047, 1026. HRMS: found 956.47361 $[C_{61}H_{66}NO_9+Na]^+$, calculated for $[C_{61}H_{66}NO_9+Na]^+$ 956.47321.

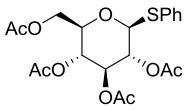
4-*O*-(β-D-Glucopyranosyl)-1-deoxynojirimycin (49):



49 was synthesised from **48** (1.00 g, 1.04 mmol) according to the procedure described for the preparation for compound **24**, to gain **49** (0.22 g, 0.67 mmol, 65% yield) as a light yellow oil. ^{1}H NMR (600 MHz, D_2O) δ 4.46 (d, *J* = 7.9 Hz, 1H, H-1'), 3.88 (dd, *J* = 12.3, 3.1 Hz, 1H, H-6a), 3.84 (dd, *J* =12.4, 2.2 Hz, 1H, H-6'a), 3.66 (dd, *J* = 12.4, 5.7 Hz, 1H, H-6'b), 3.66 – 3.62 (m, 1H, H-2), 3.62 (dd, *J* = 10.4, 8.9 Hz, H-5'), 3.49 (t, *J* = 9.1 Hz, 1H, H-3), 3.42 (t, *J* = 9.5 Hz, 1H, H-3'), 3.42 – 3.39 (m, 1H, H-5), 3.35 (dd, *J* = 9.8, 9.1 Hz, H-4'), 3.26 (dd, *J* = 12.7, 5.0 Hz, H-1a), 3.26 (dd, *J* = 9.4, 7.9 Hz, H-2'), 3.02 (ddd, *J* = 10.3, 5.0, 2.9 Hz, 1H, H-5), 2.70 (dd, *J* = 12.5, 11.2 Hz, 1H, H-1b). ^{13}C NMR (150 MHz, D_2O) δ 102.6 (C-1), 78.5 (C-4), 76.0 (C-5'), 75.6 (C-3'), 75.5 (C-3), 73.2 (C-2'), 69.4 (C-4'), 68.4 (C-2), 60.5 (C-6'), 59.2 (C-5), 58.4 (C-6), 46.6 (C-1). $[\alpha]^{20}_D$ = +25.3 (c = 1.0, MeOH). IR/cm^{-1}: 3302, 2966, 1636, 1558, 1203, 1161, 1022. HRMS: found 326.14464 $[C_{12}H_{23}NO_9+H]^+$, calculated for $[C_{12}H_{23}NO_9+H]^+$ 326.14456.

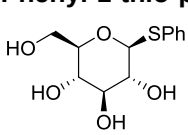
Synthesis of 2-*O*-(α-D-galactopyranpsyl-)-1-deoxynojirimycin (69)

Phenyl-1-thio-2,3,4,6-tetra-(*O*-acetyl)-β-D-glucopyranoside (51):



β-D-Glucose penta-acetate (0.996 g, 2.56 mmol) and PhSH (0.4 mL, 4 mmol) were dissolved in DCM (20 mL). The mixture was cooled to 0 °C and $BF_3{\cdot}Et_2O$ (0.46 mL, 3.7 mmol) was added dropwise. After 5 hours, TLC analysis showed complete consumption of the starting compound. The mixture was washed with sat. aq. $NaHCO_3$, organic layer was dried (Na_2SO_4), filtrated and concentrated. The crude product was purified with silica gel column chromatography to gain **51** as white crystal (1.02 g, 2.33 mmol, yield 91%). R_F = 0.7 (5:3, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.49 (m, 2H, H_{Ar} SPh), 7.36 – 7.32 (m, 3H, H_{Ar} SPh), 5.24 (t, *J* = 9.3 Hz, 1H, H-3), 5.06 (t, *J* = 9.8 Hz, 1H, H-4), 4.99 (dd, *J* = 10.1, 9.2 Hz, 1H, H-2), 4.73 (d, *J* = 10.1 Hz, 1H, H-1), 4.24 (dd, *J* = 12.3, 5.0 Hz, 1H, H-6a), 4.20 (dd, *J* = 12.3, 2.7 Hz, 1H, H-6b), 3.75 (ddd, *J* = 10.1, 5.0, 2.7 Hz, 1H, H-5), 2.11 (s, 3H, CH_3), 2.10 (s, 3H, CH_3), 2.04 (s, 3H, CH_3), 2.01 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 170.2, 169.4, 169.3 (4 x C=O), 131.6 (C_q SPh), 128.9 – 128.4 (C_{Ar} SPh), 85.7 (C-1), 75.8 (C-5), 74.0 (C-3), 69.9 (C-2), 68.2 (C-4), 62.1 (C-6), 20.7 – 20.6 (4 x CH_3).

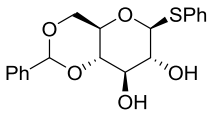
Phenyl-1-thio-β-D-glucopyranoside (52):



NaOMe (0.276 g, 5.12 mmol) was added to a solution of **51** (2.56 mmol) in MeOH (20 mL). After 24 hours, TLC analysis showed complete consumption of **51**. The solution was neutralized with amberlite H^+ resin, filtrated and

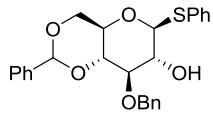
concentrated. The crude product was used for the next reaction step without further purification. R_F = 0.6 (5:1, EtOAc:MeOH). ^{1}H NMR (400 MHz, MeOD) δ 7.60 – 7.57 (m, 2H, H_{Ar} SPh), 7.35 – 7.26 (m, 3H, H_{Ar} SPh), 4.63 (d, *J* = 9.6 Hz, 1H, H-1), 3.91 (dd, *J* = 12.4, 1.6 Hz, 1H, H-6a), 3.71 (dd, *J* = 12.0, 5.6, 1H, H-6b), 3.43 (t, *J* = 8.8, 1H, H-4), 3.37 – 3.29 (m, 2H, H-3, H-5), 3.26 (dd, *J* = 9.6, 8.8, 1H, H-2). ^{13}C NMR (100 MHz, MeOD) δ 133.8 (C_q SPh), 131.3, 128.5, 127.0 (C_{Ar} SPh), 88.0 (C-1), 80.7 (C-3), 78.3 (C-4), 72.4 (C-2), 70.0 (C-5), 61.5 (C-6).

Phenyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (53):



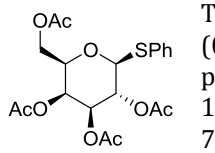
$PhCH(OMe)_2$ (5.7 mL, 38 mmol) was added to the solution of **52** (8.65 g, 31.6 mmol) in DMF (20 mL). *p*-TsOH was added to adjust the pH to 4. The mixture was heated to 60 °C and the pressure was reduced to 20 mbar. After 4.5 hours, TLC analysis showed complete consumption of **52**. The mixture was neutralized with TEA, diluted with EtOAc, washed successively with distilled water and brine, dried (Na_2SO_4), filtered, concentrated to get light yellow oil as crude product. The crude product was recrystallized from warm ethanol to get pure **53** as a white solid (19 mmol, yield 59% over two steps). R_F = 0.67 (2:1, EtOAc:PE). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.55 (m, 2H, H_{Ar} Ph), 7.59 – 7.57 (m, 3H, H_{Ar} Ph), 7.41 – 7.37 (m, 5H, H_{Ar} Ph), 5.57 (s, 1H, CH-benzylidene), 4.69 (d, *J* = 9.6 Hz, 1H, H-1), 4.44 (dd, *J* = 10.4, 4.4 Hz, 1H, H-6a) 3.91 (t, *J* = 8.8 Hz, 1H, H-3) 3.85 (dd, *J* = 7.2 Hz, 3.2 Hz, 1H, H-6b), 3.51 – 3.55 (m, 2H, H-4, H-5), 3.53 (dd, *J* = 11.8, 8.4 Hz, 1H, H-2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.8, 134.2 (C_q Ph), 133.1 – 126.3 (C_{Ar} Ph), 102.0 (C-7), 88.7 (C-1), 80.2 (C-4), 74.6 (C-3), 72.6 (C-2), 70.6 (C-5), 68.6 (C-6).

Phenyl-3-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (54):



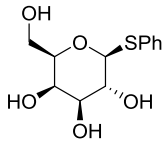
Bu_2SnO (0.35 g, 1.40 mmol) was added to a solution of **53** (0.48 g, 1.33 mmol) in toluene (17 mL), the reaction mixture was stirred overnight at 115 °C. Then toluene was evaporated, the residue was dissolved in DMF (10 mL), and CsF (0.31 g, 2.04 mmol), BnBr (0.3 mL, 2.5 mmol) was added. The reaction mixture was stirred at 115 °C for 12 hours. After TLC analysis showed complete consumption of **53**, the reaction mixture was diluted with ethyl acetate, washed successively with $NaHCO_3$ solution and brine. The organic layer was dried (Na_2SO_4), concentrated and the residue was purified with a short column (8:1, PE:EtOAc) to gain **54** (0.44 g, yield 73.3%) as light yellow crystal. R_F = 0.66 (4:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.60 (s, 1H, CH-benzylidene), 4.99 (d, *J* = 11.5 Hz, 1H, CH*H* Bn), 4.83 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.67 (d, *J* = 9.7 Hz, 1H, H-1), 4.42 (dd, *J* = 10.5, 5.0 Hz, 1H, H-6a), 3.83 (t, *J* = 10.3 Hz, 1H, H-6b), 3.76-3.63 (m, 2H, H-3, H-4), 3.58 – 3.53 (m, 2H, H-2, H-5). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2, 137.2 (C_q Ph), 133.2 – 126.0 (C_{Ar} Ph), 101.3 (CH-benzylidene), 88.5 (C-1), 81.7 (C-3), 81.1 (C-4), 74.8 (CH_2 Bn), 72.3 (C-2), 70.7 (C-5), 68.6 (C-6).

Phenyl-1-thio-2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (56):



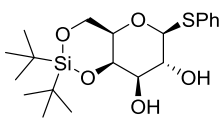
The title compound was synthesized from **55** (1.00 g, 2.56 mmol), thiophenol (0.4 mL, 3.91 mmol) and $BF_3{\cdot}Et_2O$ (0.46 mL, 3.72 mmol) according to the procedure described for the preparation of **51** to gain **56** (1.2 g, 2.5 mmol, 100%) as white crystal. R_F = 0.68 (5:3, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.52 (m, 2H, H_{Ar}), 7.34 – 7.32 (m, 3H, H_{Ar}), 5.44 (d, *J* = 3.2, 1H, H-1), 5.28 (t, *J* = 10 Hz, 1H, H-2), 5.08 (dd, *J* = 10, 3.6 Hz, 1H, H-3), 4.75 (d, *J* = 10.0 Hz, 1H, H-4), 4.23 (dd, *J* = 11.2, 7.2 Hz, 1H, H-6a), 4.15 (dd, *J* = 11.6, 6 Hz, 1H, H-6b), 3.98 (t, *J* = 6.4 Hz, 1H, H-5), 2.14 (s, 3H, CH_3), 2.11 (s, 3H, CH_3), 2.06 (s, 3H, CH_3), 1.99 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4 – 169.5 (4 x C=O), 132.6 (C_{Ar}), 132.5 (C_q Ph), 129.0, 128.2 (C_{Ar}), 86.6 (C-1), 74.4 (C-5), 72.0 (C-3), 67.3 (C-2), 67.2 (C-4), 61.7 (C-6), 20.9 (CH_3), 20.7 (CH_3), 20.7 (CH_3), 20.7 (CH_3).

Phenyl-1-thio-β-D-galactopyranoside (57):



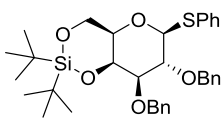
The title compound was synthesized from **57** (59.00 g, 133.95 mmol), thiophenol (0.4 mL, 3.91 mmol) and $BF_3{\cdot}Et_2O$ (0.46 mL, 3.72 mmol) according to the procedure described for the preparation of **52** to gain **57** as crude product and used in next step without further purification. R_F = 0.5 (5:1, EtOAc:MeOH). ^{1}H NMR (400 MHz, MeOD) δ 7.56 – 7.54 (m, 2H, H_{Ar} SPh), 7.31 – 7.21 (m, 3H, H_{Ar} SPh), 4.59 (d, *J* = 8.0 Hz, 1H, H-1), 3.90 (d, *J* = 4.0 Hz, 1H, H=4), 3.76 (dd, *J* = 12.0, 8.0 Hz, 1H, H-6a), 3.71 (dd, *J* = 12.0, 4 Hz, 1H, H-6b), 3.59 – 3.55 (m, 2H, H-5, H-2), 3.50 (dd, *J* = 12.0, 4 Hz, 1H, H-3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 130.1 (C_q SPh), 132.1 – 128.0 (C_{Ar} SPh), 90.3 (C-1), 80.6 (C-3), 76.3 (C-4), 71.0 (C-2), 70.4 (C-5), 62.6 (C-6).

Phenyl-4,6-*O*-di-*tert*-butylsilylene-1-thio-β-D-galactopyranoside (58):



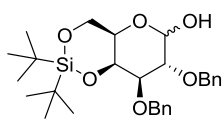
57 (3.12 g, 11.5 mmol) was co-evaporated with DMF. The mixture was dissolved in pyridine (20 mL). The solution was cooled to -20 °C and *t*BuSi(OTf)$_2$ (3.5 mL, 9.9 mmol) was added. After 2 hours, TLC analysis showed complete consumption of **57**. Methanol was added to quench the reaction. The volatiles were evaporated and the residue was diluted with EtOAc, washed with HCl (1M) and sat. aq. $NaHCO_3$. The organic layer was dried (Na_2SO_4), filtrated and concentrated. The residue was purified with silica gel column chromatography (1:4 → 1:3, EtOAc:PE) to gain **52** (2.49 g, 6.04 mmol, yield 53%) as light yellow oil. R_F = 0.34 (1:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.52 (m, 2H, H_{Ar} SPh), 7.39 – 7.30 (m, 3H, H_{Ar} SPh), 4.58 (d, *J* = 9.8 Hz, 1H, H-1), 4.46 (dd, *J* = 3.5, 1.1 Hz, 1H, H-4), 4.29 (dd, *J* = 2.0, 1.1 Hz, 2H, H_2-6), 3.77 (dd, *J* = 9.8, 8.9 Hz, 1H, H-2), 3.56 (dd, *J* = 8.9, 3.5 Hz, 1H, H-3), 3.50 (td, *J* = 2.0, 1.1 Hz, 1H, H-5), 1.08 (s, 9H, 3 x CH_3, *tert*-Bu), 1.06 (s, 9H, 3 x CH_3, *tert*-Bu). ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.1 (C_q), 132.6 – 127.9 (C_{Ar} SPh), 89.1 (C-1), 75.2 (C-5), 75.1 (C-3), 72.5 (C-4), 70.7 (C-2), 67.1 (C-6), 27.6 – 20.7 (6 x CH_3, *tert*-Bu).

Phenyl-2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-1-thio-β-D-galactopyranoside (59):



58 (15.74 g, 38.15 mmol) was dissolved in DMF (20 mL). BnBr (9 mL, 76 mmol) and TBAI (16.75 g, 68.68 mmol) were added. The mixture was cooled to 0 °C and NaH (8.2 g, 0.21 mmol) was added in small potions. After an overnight reaction, TLC analysis showed complete consumption of **58**. The mixture was quenched by the addition of water, diluted with EtOAc and washed with brine. The organic layer was dried (Na_2SO_4), filtrated and concentrated. The residue was purified with silica gel column chromatography (20:1 → 10:1, PE:EtOAc) to gain **59** (12.66 g, 21.35 mmol, yield 56%) as thick oil. R_F = 0.4 (5:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.27 (m, 12H, H_{Ar} Bn/SPh), 4.94 (s, 2H, CH_2 Bn), 4.80 (q, *J* = 12 Hz, 2H, CH_2 Bn), 4.71 (d, *J* = 9.6 Hz, 1H, H-1), 4.53 (d, *J* = 2.8 Hz, 1H, H-4), 4.24 (m, 2H, H_2-6), 3.89 (t, *J* = 9.6 Hz, 1H, H-2), 3.52 (dd, *J* = 9.2, 3.2 Hz, 1H, H-3), 3.32 (s, 1H, H-5), 1.17 (s, 9H, 3 x CH_3, *tert*-Bu), 1.12 (s, 9H, 3 x CH_3, *tert*-Bu). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 134.9 (C_q Bn), 132.1 – 127.3 (CH_{Ar} Bn/SPh), 88.7 (C-1), 82.8 (C-3), 77.0 (C-2), 76.0 (CH_2 Bn), 74.8 (C-5), 71.1 (CH_2 Bn), 70.0 (C-4), 67.4 (C-6), 27.7, 27.7 (CH_3, *tert*-Bu), 23.5 (C_q, *tert*-Bu), 20.8 (C_q, *tert*-Bu).

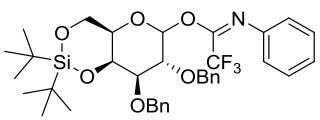
2,3-Di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-D-galactopyranoside (60):



59 (0.61 g, 1.0 mmol) was co-evaporated with toluene (3 x) and dissolved in DCM (50 mL). The solution was cooled to 0 °C. *N*-Iodosuccinimide (0.227 g, 1.03 mmol) and TFA (77 µL, 1.0 mmol) were added to the solution. After 1 hour, TLC analysis showed complete consumption of **59**. The reaction was quenched by adding TEA, and sat. aq. $Na_2S_2O_3$ was added to the mixture. The mixture was extracted with EtOAc, and the organic layer was dried (Na_2SO_4), filtrated and concentrated. The resulting residue was purified with silica gel column chromatography (10:1

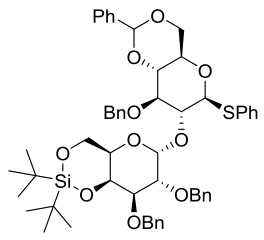
→ 2:1, PE:EtOAc) to gain **60** (0.451 g, 0.903 mmol, yield 88%). R_F = 0.28 (toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.29 (m, 10H, H_{Ar} Bn), 5.23 (d, *J* = 3.6 Hz, 1H, H-1), 4.92 (d, *J* = 11.6 Hz, 2H, CH_2 Bn), 4.81 – 4.72 (m, 2H, CH_2 Bn), 4.54 (d, *J* = 3.0 Hz, 1H, H-4), 4.21 – 4.12 (m, 2H, H_2-6), 4.02 (dd, *J* = 9.6, 3.6 Hz, 1H, H-2), 3.87 (d, *J* = 3.2 Hz, 1H, H-5), 3.84 (d, *J* = 2.8 Hz, 1H, H-3), 1.12 (s, 9H, 3 x CH_3, *tert*-Bu), 1.08 (s, 9H, 3 x CH_3, *tert*-Bu). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 138.3 (C_q Bn), 128.4 – 127.6 (CH_{Ar} Bn), 92.1 (C-1), 77.5 (C-3), 74.8 (C-2), 74.8 (CH_2 Bn), 71.0 (C-4), 71.0 (CH_2 Bn), 67.4 (C-6), 67.3 (C-5), 27.7 (CH_3), 27.7 (CH_3), 27.6, 27.4 (CH_3, *tert*-Bu), 23.5, 20.7 (C_q, *tert*-Bu).

2,3-Di-*O*-benzoyl-4,6-*O*-di-*tert*-butylsilanediyl-D-galactopyranoside-*N*-phenyl-2,2,2-trifluoroacetimidate (61):



Cs_2CO_3 (0.28 g, 0.85 mmol) and trifluoro-phenylacetimidoyl chloride (0.20 g, 0.96 mmol) was added to a solution of **60** (0.27 g, 0.54 mmol) in acetone (3 mL). The reaction mixture was kept at 0 °C under argon atmosphere. After 3 hours, the reaction mixture was filtrated through a pad of Celite. The filtrate was concentrated and purified on a short column (20:1 → 2:1, PE:EtOAc) to get **61** (0.22 g, 0.26 mmol, yield 65%) as anomeric mixture at ratio 1:1. R_F = 0.56, 0.38 (10:1, PE:EtOAc). For the upper spot on TLC, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 – 6.78 (m, 15H, H_{Ar} Bn/Ph), 6.55 (br s, 1H, H-1), 4.89 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.85 – 4.72 (m, 3H, 3 x CH*H* Bn), 4.62 (br s, 1H, H-4), 4.33 – 4.18 (m, 3H, H_2-6, H-2), 3.91 (d, *J* = 10.1 Hz, 1H, H-3), 3.81 (br s, 1H, H-5), 1.10 (s, 9H, 3 x CH_3, *tert*-Bu), 1.02 (s, 9H, 3 x CH_3, *tert*-Bu). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1 (C=N), 143.8, 138.6, 138.2 (C_q Bn), 129.1 – 120.6 (CH_{Ar} Bn), 100.0 (CF_3), 94.8 (H-1), 77.3 (C-3), 73.7 (CH_2 Bn), 73.6 (C-2), 71.1 (CH_2 Bn), 70.7 (C-4), 70.0 (C-5), 66.8 (C-6), 27.6, 27.2 (CH_3, *tert*-Bu), 23.5, 20.7 (C_q, *tert*-Bu).

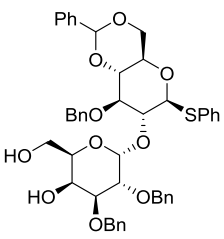
3-Benzyl-4,6-*O*-benzylidene-2-*O*-(2,3-di-benzyl-4,6-*O*-di-*tert*-butylsilyl-galactopyranpsyl)-1-thio-D-glucopyranose (62):



54 (0.405 g, 0.899 mmol) and **61** (1.201 g, 1.788 mmol) were co-evaporated with toluene (3 x). The residue was dissolved in dried DCM (4 mL) and cooled to 0 °C, followed by dropwise addition of trimethylsilyl trifluoromethanesulfonate (0.045 mL, 0.25 mmol). After an overnight reaction, TLC analysis showed complete consumption of **61**. The reaction was quenched by the addition of TEA and concentrated. The resulting residue was purified with silica gel column chromatography (40:1 → 10:1, PE:EtOAc). Yield 69% (0.56 g, 0. 61 mmol). R_F = 0.15 (10:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.04 (m, 25H, H_{Ar}), 5.89 (d, *J* = 4 Hz, 1H, H-1'), 5.65 (s, 1H, CH-benzylidene), 5.09 (d, *J* = 10 Hz, 1H, CH*H Bn*), 4.97 (d, *J* = 9.2 Hz, 1H, H-1), 4.89 (s, 2H, CH_2 Bn), 4.81 (q, *J* = 12 Hz, 2H, CH_2 Bn), 4.43 (dd, *J* = 10.8, 5.2 Hz, 1H, H-6a), 4.33 (d, *J* = 10.4 Hz, 1H, CH*H* Bn), 4.07 (dd, *J* = 10.0, 3.6 Hz, 1H, H-2'), 4.02 (d, *J* = 8.0 Hz, 1H, H-4'), 3.89 – 3.72 (m, 6H, H-3, H-2, H-5', H-6b, H-3', H-4), 3.56 (dd, *J* = 12.8, 1.6 Hz, 1H, H-6'a), 3.60 – 3.53 (m, 1H, H-5), 3.02 (dd, *J* = 12.6, 2.2 Hz, 1H, H-6'b), 1.02 (s, 9H, CH_3, *tert*-Bu), 0.99 (s, 9H, CH_3, *tert*-Bu). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.5 – 126.0 (C_{Ar}), 101.1 (CH-benzylidene), 96.2 (C-1'), 87.6 (C-1'), 82.2 (C-3), 81.0 (C-4), 77.0 (C-3'), 76.2 (CH_2 Bn), 74.2 (C-2'), 73.7 (CH_2 Bn), 72.7 (C-2), 71.2 (CH_2 Bn), 71.0 (C-4'), 70.0 (C-5), 68.7 (C-6), 66.9 (C-3'), 66.5 (C-6'), 27.7, 27.3 (CH_3, *tert*-Bu), 23.3 (C_q, *tert*-Bu), 20.6 (C_q, *tert*-Bu).

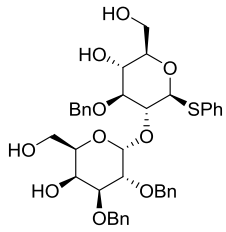
Phenyl-1-thio-2-*O*-(2,3-di-*O*-benzyl-α- galactopyranosyl)-3-benzyl-4,6-*O*-benzylidene-D-glucopyranose (63):

TBAF (1M in THF, 1.2 mL, 1.2 mmol) was added dropwise to a solution of **62** (0.16 g, 0.17 mmol) in THF (2 mL) at 0 °C, and the yellow solution was stirred at room temperature overnight. The reaction mixture was then diluted with EtOAc, washed with brine, dried (Na_2SO_4), filtered and concentrated. The residue was purified with silica gel column



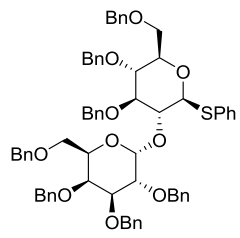
chromatography (5:2 → 1:1, PE:EtOAc) to get pure **63** (0.11 g, 0.14 mmol, yield 82%). R_F = 0.17 (5:2, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.17 (m, 25H, H_{Ar}), 6.01 (d, *J* = 3.8 Hz, 1H, H-1'), 5.63 (s, 1H, CH-benzylidene), 5.10 (d, *J* = 10.7 Hz, 1H, CH*H* Bn), 4.96 (d, *J* = 9.3 Hz, 1H, H-1), 4.87 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.84 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.77 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.71 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.48 (d, *J* = 10.7 Hz, 1H, CH*H* Bn), 4.41 (dd, *J* = 10.5, 5.0 Hz, 1H, H-6a), 4.06 (t, *J* = 4.8 Hz, 1H, H-5'), 3.96 – 3.90 (m, 3H, H-2, H-2', H-3), 3.84 (d, *J* = 10.2 Hz, 1H, H-6b), 3.81 – 3.78 (m, 1H, H-4), 3.75 (dd, *J* = 10.0, 3.2 Hz, 1H, H-3'), 3.59 (dd, *J* = 3.2, 1.5 Hz, 1H, H-4'), 3.55 (dt, *J* = 9.8, 4.8 Hz, 1H, H-5), 3.30 (dd, *J* = 11.8, 5.4 Hz, 1H, H-6'a), 3.23 (dd, *J* = 11.8, 4.3 Hz, 1H, H-6'b). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.9 – 125.9 (C_{Ar}), 101.1 (CH-benzylidene), 95.7 (C-1'), 87.5 (C-1), 82.0 (C-4), 81.9 (C-3) 76.7 (C-3'), 76.0 (CH_2 Bn), 75.4 (C-2'), 73.3 (CH_2 Bn), 73.2 (C-2), 72.8 (CH_2 Bn), 70.0 (C-5), 69.9 (C-4'),68.6 (C-6), 68.4 (C-5'), 63.1 (C-6'). $[\alpha]^{20}_D$ = +22.1 (c = 0.85, $CHCl_3$). HRMS: found 815.28588 $[C_{46}H_{48}O_{10}S+Na]^+$, calculated for $[C_{46}H_{48}O_{10}S+Na]^+$ 815.28604.

Phenyl-1-thio-2-*O*-(2,3-di-*O*-benzyl-α-galactopyranosyl)-3-benzyl-D-glucopyranose (64):



p-Toluenesulfonic acid monohydrate (0.065 g, 0.34 mmol) was added to a solution of **63** (0.10 g, 0.13 mmol) in methanol and DCM (10 mL, 1:1, v/v), and the reaction mixture was kept stirred at room temperature overnight. After quenching by the addition of TEA, the reaction mixture was concentrated and purified with silica gel column chromatography (1:1, pentane: EtOAc) to give **64** (0.08 g, yield 90%). R_F = 0.1 (1:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.16 (m, 15H, H_{Ar}), 5.97 (d, *J* = 3.7 Hz, 1H, H-1'), 5.06 (d, *J* = 11.2 Hz, 1H, CH*H* Bn), 4.91 (d, *J* = 9.7 Hz, 1H, H-1), 4.87 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.82 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.76 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.71 (d, *J* = 11.7 Hz, 1H, CH*H* Bn), 4.58 (d, *J* = 11.2 Hz, 1H, CH*H* Bn), 4.05 (td, *J* = 5.2, 4.7, 2.3 Hz, 1H, H-5'), 3.93 (dd, *J* = 10.1, 3.9 Hz, 1H, H-2'), 3.90 – 3.79 (m, 4H, H-6a, H-2, H-6b, H-3), 3.76 (dd, *J* = 10.0, 3.2 Hz, 1H, H-3'), 3.66 (t, *J* = 9.0 Hz, 1H, H-4), 3.54 (d, *J* = 2.9 Hz, 1H, H-4'), 3.42 – 3.34 (m, 2H, H-6'a, H-5), 3.26 (dd, *J* = 11.8, 4.0 Hz, 1H, H-6'b). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.1 – 126.3 (C_{Ar}), 95.5 (C-1'), 87.4 (C-1), 85.4 (C-4), 79.3 (C-5), 76.6 (C-3'), 76.2 (CH_2 Bn), 75.4 (C-2'), 73.2 (CH_2 Bn), 73.1 (C-2), 72.7 (CH_2 Bn), 71.1 (C-3), 69.1 (C-4'), 68.6 (C-5'), 62.9 (C-6'), 62.0 (C-6). $[\alpha]^{20}_D$ = +16.3 (c = 2.45, $CHCl_3$). HRMS: found 727.25414 $[C_{39}H_{44}O_{10}+Na]^+$, calculated for $[C_{39}H_{44}O_{10}+Na]^+$ 727.25474.

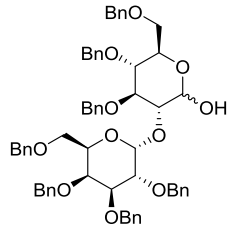
Phenyl-1-thio-2-*O*-(2,3,4,6-tetra-*O*-benzyl-α-galactopyranosyl)-3,4,6-tri-benzyl-D-glucopyranose (65):



NaH (60% on mineral oil, 48.8 mg, 1.22mmol) was added to a solution of **64** (0.08 g, 0.11 mmol) in DMF (1 mL) at 0 °C under argon atmosphere, the suspension was stirred at 0 °C for 1 hour. Then BnBr (0.067 mL, 0.56 mmol) was added. The reaction mixture was kept stirred at room temperature overnight. After quenched by the addition of water, the reaction mixture was extracted with EtOAc, washed with water and brine, dried (Na_2SO_4), filtered, concentrated and purified with silica gel column chromatography (20:1, pentane:EtOAc) to get pure **65** (0.11g, 0.10 mmol, yield 92%). R_F = 0.62 (5:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.09 (m, 40H, H_{Ar}), 6.01 (d, *J* = 3.7 Hz, 1H, H-1'), 4.98 (d, *J* = 11.6 Hz, 1H, CH*H* Bn), 4.92 – 4.53 (m, 10H, 5 x CH_2 Bn), 4.49 (d, *J* = 11.4 Hz, 1H, CH*H* Bn), 4.33 (t, *J* = 6.5 Hz, 1H, H-5'), 4.30 (d, *J* = 12.0 Hz, 1H, CH*H* Bn), 4.22 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.12 (dd, *J* = 10.2, 3.6 Hz, 1H, H-2'), 3.97 (t, *J* = 9.1 Hz, 1H, H-2), 3.89 (dd, *J* = 10.2, 2.7 Hz, 1H, H-3'), 3.81 – 3.72 (m, 3H, H_2-6, H-4), 3.65 (t, *J* = 9.3 Hz, 1H, H-3), 3.60 (dd, *J* = 2.9, 1.3 Hz, 1H, H-4'), 3.55 (ddd, *J* = 9.8, 4.5, 2.1 Hz, 1H, H-5), 3.44 (dd, *J* =

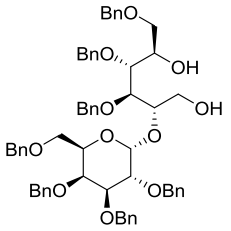
9.5, 6.4 Hz, 1H, H-6'a), 3.28 – 3.23 (m, 1H, H-6'b). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9 – 127.1 (C_{Ar}), 95.6 (C-1'), 87.1 (C-1), 85.2 (C-4), 79.0 (C-5), 78.5 (C-3), 78.3 (C-3'), 76.3 (C-2'), 75.5 (CH_2 Bn), 75.2 (C-4'), 74.9 (CH_2 Bn), 74.7 (CH_2 Bn), 73.5 (CH_2 Bn), 73.4 (C-2), 73.1 (CH_2 Bn), 73.0 (CH_2 Bn), 69.3 (C-5'), 69.1 (C-6'), 68.9 (C-6).

2-*O*-(2,3,4,6-Tetra-*O*-benzyl-α-galactopyranpsyl)-3,4,6-tri-*O*-benzyl-D-glucopyranose (66):



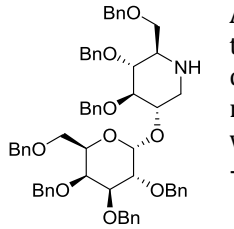
NIS (0.13 g, 0.53 mmol) and TFA (35 µL) was added to a solution of **65** (0.44 g, 0.41 mmol) in dried DCM (5 mL) at 0 °C under argon atmosphere. The reaction was stirred at room temperature for 2 hours. Piperidine was added to quench the reaction at 0 °C, after which sat. aq. $Na_2S_2O_3$ solution was added. The reaction mixture was extracted with EtOAc, washed with HCl solution (1M) and brine. The organic layer was dried (Na_2SO_4), filtered and concentrated. The crude product was purified with silica gel column chromatography (4:1 → 2:1, PE:EtOAc) to gain pure **66** (0.28 g, 0.29 mmol, yield 71%) as a mixture of two isomers (2:5). R_F = 0.3 (4:1, PE:EtOAc). For the major isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.34 (d, *J* = 3.4 Hz, 1H, H-1'), 4.99 – 4.50 (m, 13H, 6 x CH_2 Bn, H-1), 4.41 – 4.28 (m, 2H, CH_2 Bn), 4.15 (d, *J* = 7.2 Hz, 1H, H-5), 4.12 – 4.05 (m, 2H, H-5', H-2), 4.00 – 3.89 (m, 3H, H-4, H-4', H-3'), 3.85 (dd, *J* = 9.0, 3.4 Hz, 1H, H-2'), 3.83 – 3.70 (m, 3H, H_2-6', H-3), 3.49 – 3.45 (m, 2H, H_2-6). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7 – 127.5 (C_{Ar}), 96.5 (C-1), 90.3 (C-1'), 80.3 (C-4), 79.0 (C-4'), 77.5 (C-3), 77.3 (CH_2 Bn), 75.4 (C-2'), 75.3 (CH_2 Bn), 74.8 (CH_2 Bn), 74.5 (C-2), 74.3, 73.6, 73.2, 72.5 (4 x CH_2 Bn), 70.9 (C-5'), 69.7 (C-5), 68.6 (C-6'), 68.5 (C-6).

2-*O*-(2,3,4,6-Tetra-*O*-benzyl-α-galactopyranosyl)-3,4,6-tri-*O*-benzyl-D-glucitol (67):



$LiAlH_4$ (0.5 mL, 2.4 M in THF, 1.2 mmol) was added dropwise into a solution of **66** (0.25 g, 0.26 mmol) in THF (3 mL) at 0 °C under argon atmosphere. After stirred overnight, the reaction mixture was slowly quenched by the addition of methanol, after which HCl (1M, 3 mL) was added. Then the mixture was diluted with ethyl acetate and washed with brine, the water layer was reextracted with EtOAc. The organic layers were combined, dried (Na_2SO_4), filtered and concentrated. The crude product was purified with silica gel column chromatography (2:1 → 1:1, PE:EtOAc) to gain **67** (0.22 g, 0.23 mmol, yield 88%). R_F = 0.58 (1:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.05 (d, *J* = 3.5 Hz, 1H, H-1'), 4.96 – 4.86 (m, 2H, CH_2 Bn), 4.79 – 4.51 (m, 6H, 3 x CH_2 Bn), 4.45 (d, *J* = 12.0 Hz, 1H, CH*H* Bn), 4.35 (d, *J* = 12.0 Hz, 1H, CH*H* Bn), 4.14 – 4.04 (m, 2H, H-2, H-5'), 4.11 (dd, *J* = 10.1, 3.7 Hz, 1H, H-2'), 4.00 – 3.98 (m, 1H, H-5), 3.98 (dd, *J* = 10.1, 2.6 Hz, 1H, H-3') 3.92 – 3.82 (m, 3H, H-3, H-4', H-4), 3.81 – 3.76 (m, 1H, H-6a), 3.76 – 3.71 (m, 2H, H_2-6'), 3.69 – 3.64 (m, 1H, H-6b), 3.52 (dd, *J* = 9.3, 6.7 Hz, 1H, H-1a), 3.38 (dd, *J* = 9.4, 5.8 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5 – 127.5 (C_{Ar}), 99.9 (C-1'), 81.8 (C-5), 79.3 (C-3'), 79.2 (C-4'), 79.2 (C-3), 76.2 (C-2'), 74.7 (C-4), 74.6 – 72.6 (7 x CH_2 Bn), 71.2 (C-6'), 70.7 (C-5'), 70.4 (C-2), 69.4 (C-1), 62.5 (C-6). $[\alpha]^{20}_D$ = +39.1 (c = 1.17, $CHCl_3$). HRMS: found 997.44983 $[C_{61}H_{66}O_{11}+Na]^+$, calculated for $[C_{61}H_{66}O_{11}+Na]^+$ 997.44973.

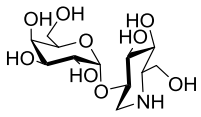
2-*O*-(2,3,4,6-Tetra-*O*-benzyl-α-galactopyranpsyl)-3,4,6-tri-*O*-benzyl-1-deoxynojirimycin (68):



A solution of $(COCl)_2$ (100 µL, 1.16 mmol) in dry DCM (1.5 mL) was cooled to -78 °C under argon atmosphere. DMSO (100 µL, 1.40 mmol) dissolved in dry DCM (1.5 mL) was added dropwise. After 40 minutes **67** (0.32 g, 0.33 mmol, which was co-evaporated with toluene 3 x), in dry DCM (7.5 mL), was added dropwise to the mixture. The reaction was stirred for 2 hours at -78 °C, after which Et_3N (0.51 mL, 3.65 mmol) was added dropwise. The

mixture was gradually warmed to -40 °C in more than 1 hour, after which it was poured into a cooled (0 °C) MeOH solution (60 mL) containing $NaCNBH_3$ (0.09 g, 1.44 mmol), $HCOONH_4$ (0.49 g, 7.76 mmol), and Na_2SO_4 (0.19 g, 1.34 mmol). The mixture was stirred overnight allowing the reaction to reach room temperature. TLC analysis showed the formation of the product (2:1, PE:EtOAc, R_F = 0.37). After filtration, the volatiles were evaporated, as the residue was dissolved in EtOAc (100 mL). The solution was washed with sat. aq. $NaHCO_3$ solution, dried (Na_2SO_4) filtered and concentrated. The residue was purified with silica gel column chromatography (5:1 → 2:3, PE:EtOAc) to give **62** in 24% yield (0.07 g, 0.073 mmol). R_F = 0.37 (2:1, PE:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.95 – 4.80 (m, 7H, H-1', 3 x CH_2 Bn), 4.72 (d, *J* = 11.8 Hz, 1H, CH*H* Bn), 4.67 (d, *J* = 12.1 Hz, 1H, CH*H* Bn), 4.57 – 4.44 (m, 4H, 2 x CH_2 Bn), 4.31 (d, *J* = 6.2 Hz, 2H, CH_2 Bn), 4.20 (td, *J* = 6.5, 1.3 Hz, 1H, H-5'), 4.05 (dd, *J* = 10.1, 3.6 Hz, 1H, H-2'), 3.89 (dd, *J* = 10.1, 2.9 Hz, 1H, H-3'), 3.75 (dd, *J* = 9.2, 4.6 Hz, 1H, H-2), 3.72 – 3.69 (m, 2H, H-6a, H-4'), 3.65 – 3.59 (m, 1H, H-6b), 3.60 (t, *J* = 9.2 Hz, 1H, H-3), 3.52 (dd, *J* = 9.6, 6.4 Hz, 1H, H-6'a), 3.41 (t, *J* = 9.3 Hz, 1H, H-4), 3.32 (dd, *J* = 9.6, 6.6 Hz, 1H, H-6'b), 3.25 (dd, *J* = 12.5, 4.8 Hz, 1H, H-1a), 2.76 (ddd, *J* = 9.3, 5.0, 2.6 Hz, 1H, H-5), 2.56 (dd, *J* = 12.5, 10.4 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.8 – 127.5 (C_{Ar}), 94.5 (C-1'), 85.9 (C-3), 80.4 (C-4), 78.7 (C-3'), 76.5 (C-2'), 75.6 (CH_2 Bn), 75.2 (C-4'), 75.2 (CH_2 Bn), 74.8 (CH_2 Bn), 74.8 (C-2), 73.7 (CH_2 Bn), 73.5 – 72.9 (4 x CH_2 Bn), 69.8 (C-6), 68.9 (C-6'), 68.8 (C-5'), 59.7 (C-5), 46.5 (C-1). $[\alpha]^{20}_D$ = +76.9 (c = 0.32, $CHCl_3$). HRMS: found 956.47350 $[C_{61}H_{65}NO_9+H]^+$, calculated for $[C_{61}H_{65}NO_9+H]^+$ 956.47321.

2-*O*-(α-D-galactopyranpsyl-)-1-deoxynojirimycin (69):



62 (0.2 g, 0.21 mmol) was dissolved in ethanol (6 mL), pH of the solution was adjusted to 2 with 1M HCl. Pd/C (10%) was added, the mixture was shaken under H_2 atmosphere at 4 bar for 24 hours. The catalyst was filtered through a pad of Celite and the filtrate was concentrated. The residue was purified on size exclusion column chromatography (eluent: NH_4Ac, 0.15 M, aq.) to get pure **69** (35 mg, 0.11 mmol, yield 52%). ^{1}H NMR (400 MHz, D_2O) δ 4.93 (d, *J* = 3.8 Hz, 1H, H-1'), 4.05 (t, *J* = 6.4 Hz, 1H, H-5'), 3.85 (d, *J* = 3.2 Hz, 1H, H-4'), 3.80 (dd, *J* = 12.8, 3.1 Hz, 1H, H-6a), 3.77 – 3.70 (m, 3H, H-6b, H-2, H-3'), 3.68 (dd, *J* = 10.5, 3.7 Hz, 1H, H-2'), 3.58 (d, *J* = 6.2 Hz, 2H, H-6'), 3.54 (dd, *J* = 12.6, 5.0 Hz, 1H, H-1a), 3.52 – 3.49 (m, 2H, H-3, H-4), 3.06 (ddt, *J* = 8.0, 5.4, 3.1 Hz, 1H, H-5), 2.84 (dd, *J* = 12.5, 11.5 Hz, 1H, H-1b). ^{13}C NMR (100 MHz, D_2O) δ 100.0 (C-1'), 74.4 (C-3), 71.6 (C-3'), 70.9 (C-5'), 69.0 (C-2), 69.0 (C-4'), 67.8 (C-2'), 67.6 (C-4), 60.8 (C-6'), 59.8 (C-5), 57.6 (C-6), 43.2 (C-1). HRMS: found 364.10099 $[C_{12}H_{23}NO_9+K]^+$, calculated for $[C_{12}H_{23}NO_9+K]^+$ 364.10044.

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