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Synthesis of Glycosylated 1-Deoxynojirimycins Starting from Natural and Synthetic Disaccharides

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Abstract: Iminosugars are an important class of natural products and have been subject to extensive studies in organic synthesis, bioorganic chemistry and medicinal chemistry, yet only a limited number of these studies are on glycosylated iminosugars. Here, a general route of synthesis is presented towards glycosylated 1-deoxynojirimycin derivatives based on the oxidation–reductive amination protocol that in the past has also been shown to be a versatile route towards 1-deoxynojirimycin. The strategy can be applied on commercial disaccharides, as shown in four examples, as well as on disaccharides that are not commercially available and are synthesized for this purpose, as shown by a fifth example.

Introduction

Iminosugars have received considerable interest in the past decades because of their potential to inhibit glycoprocessing enzymes.[1] A relatively unexplored class of iminosugars comprises the glycosylated deoxynojirimycin derivatives. Whereas monosaccharide iminosugars 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. Glycosylated iminosugars have been isolated from plants and microorganisms, often organisms that also produce 1-deoxynojirimycin (DNJ).[2] However, the natural abundance of such glycosylated iminosugars is often quite low, and 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;[3] 2) chemical glycosylation[4] of DNJ derivatives and 3) strategies[5] based on disaccharide (or oligosaccharide) entities as starting material. The enzymatic glycosylation of DNJ derivatives has been accomplished using glycohydrolases as catalysts in transglycosylation of an appropriate donor glycoside. One of the earliest endeavors in this vein comprises the synthesis of *malto*-DNJ using α-cyclodextrin as glucose donor and *bacillus macerans* amylase as transglycosylase.[3a] Following these studies, it was shown that a variety of alternative glycosides including *p*-nitrophenyl-α-D-galactose,[3b] UDP-glucose,[3c] and lactose[3d] are effective donor glycosides as well, expanding the methodology to yield a variety of glycosylated DNJ derivatives. Enzymatic approaches hold several advantages, including mild reaction conditions, readily available starting materials 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, a mixture of glycosylated DNJs was obtained.[3e] Because of their similar chemical and physical properties, separation of such a mixture can be a challenge. Chemical glycosylation forms an attractive alternative for enzymatic glycosylation of DNJ.[4] In chemical glycosylation approaches, part of the hydroxyl groups in the acceptor (DNJ) are selectively protected, leaving the hydroxyl to be modified available for glycosylation using an appropriate donor 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 long and tedious. The third conceptual strategy towards glycosylated DNJ derivatives that has been studied to some extent comprises the use of disaccharides as starting material.[5] 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 work is rooted in the double reductive amination strategy earlier applied by us,[6] and others,[7] for the synthesis of DNJ. 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,

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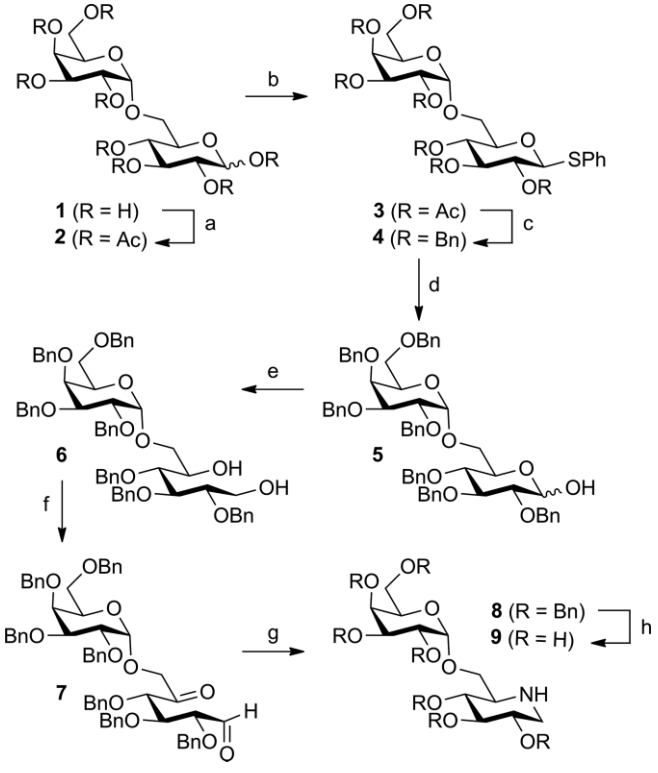
which in a double reductive amination event is transformed into the target glycosylated DNJ derivative. An important feature of this Scheme is the recovery of the stereo-center at C5 of the newly formed iminosugar, which works well when the glucopyranose configuration is the desired one.

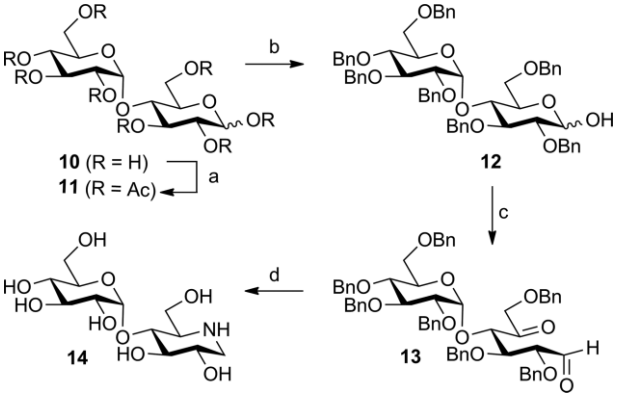
Results and Discussion

The synthesis of 6-*O*-(α-D-galactopyranosyl)-1-deoxynojirimycin (**9**, 1-deoxy-*melibio*-DNJ) is depicted in Scheme 1 and reveals the general strategy we also applied for the preparation of the ensuing aza-disaccharides (**14**, **19**, **24** and **29**, see Scheme 2, Scheme 3, Scheme 4 and Scheme 5, respectively).

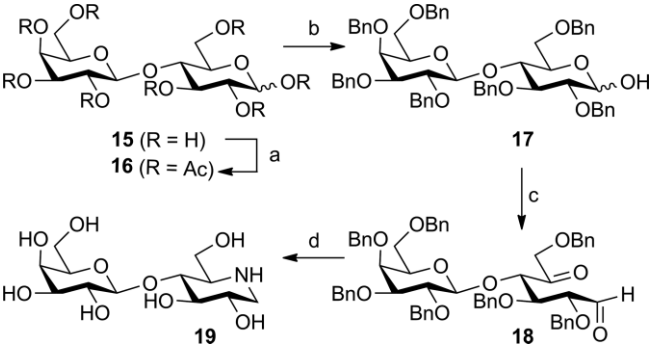


Scheme 1. Reagents and conditions: a) Ac_2O, NaOAc, reflux, 90 %. b) PhSH, $BF_3{\cdot}OEt_2$, CH_2Cl_2, 82 %. c) 1) NaOMe, MeOH; 2) NaH, BnBr, DMF, 50 % over the two steps. d) NIS, TFA, CH_2Cl_2, 77 %. e) $LiAlH_4$, THF, 74 %. f) oxalyl chloride, DMSO, Et_3N, –78 °C. g) HCO_2NH_4, Na_2SO_4, $NaCNBH_3$, h) H_2, Pd/C (10 %), DMF/MeOH, HCl (aq), 50 % over the three steps.

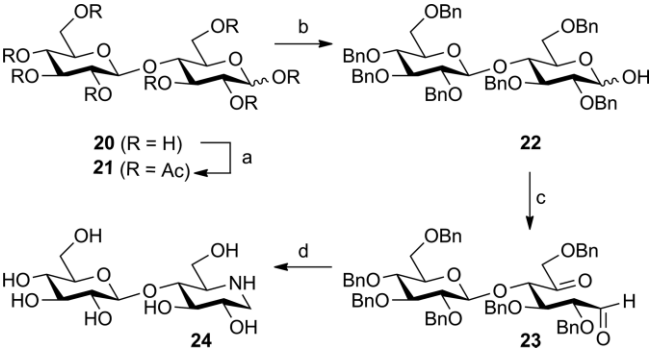
Treatment of melibiose **1**, which is commercially available, with sodium acetate in refluxing acetic anhydride afforded peracetylated melibiose **2**, which was treated with thiophenol and $BF_3{\cdot}OEt_2$ to give phenylthiomelibioside **3** in 74 % yield over the two steps. Zémplen deacetylation followed by benzylation yielded perbenzylated thiomelibiose **4**, the thiophenyl group in which could be removed using conditions we developed previously[8] (treatment with *N*-iodosuccinimide and trifluoroacetic acid) to yield lactol **5** as the key intermediate in 39 % yield over the three steps. In the next step, the hemiacetal moiety in **5** was reduced (lithium aluminum hydride) to give diol **6**, which was oxidized to keto-aldehyde **7** using Swern conditions. Double reductive amination with concomitant regeneration of the chiral center at C-5 (DNJ ring, glucopyranose numbering) was



Scheme 2. Reagents and conditions: a) Ac_2O, NaOAc, reflux, 94 %. b) 1) PhSH, $BF_3{\cdot}OEt_2$, CH_2Cl_2; 2) NaOMe, MeOH; 3) NaH, BnBr, DMF; 4) NIS, TFA, CH_2Cl_2, 50 % over the four steps. c) 1) $LiAlH_4$, THF; 2) oxalyl chloride, DMSO, Et_3N, –78 °C. d) HCO_2NH_4, Na_2SO_4, $NaCNBH_3$; 2) H_2, Pd/C (10 %), DMF/MeOH, HCl (aq), 23 % over the four steps.

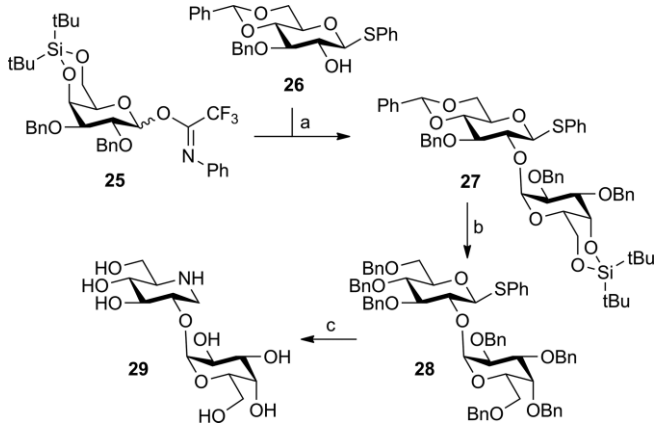


Scheme 3. Reagents and conditions: a) Ac_2O, NaOAc, reflux, 100 %. b) 1) PhSH, $BF_3{\cdot}OEt_2$, CH_2Cl_2; 2) NaOMe, MeOH; 3) NaH, BnBr, DMF; 4) NIS, TFA, CH_2Cl_2, 65 % over the four steps. c) 1) $LiAlH_4$, THF; 2) oxalyl chloride, DMSO, Et_3N, –78 °C. d) HCO_2NH_4, Na_2SO_4, $NaCNBH_3$; 2) H_2, Pd/C (10 %), DMF/MeOH, HCl (aq), 11 % over the four steps.



Scheme 4. Reagents and conditions: a) Ac_2O, NaOAc, reflux, 98 %. b) 1) PhSH, $BF_3{\cdot}OEt_2$, CH_2Cl_2; 2) NaOMe, MeOH; 3) NaH, BnBr, DMF; 4) NIS, TFA, CH_2Cl_2, 73 % over the four steps. c) 1) $LiAlH_4$, THF; 2) oxalyl chloride, DMSO, Et_3N, –78 °C. d) HCO_2NH_4, Na_2SO_4, $NaCNBH_3$; 2) H_2, Pd/C (10 %), DMF/MeOH, HCl (aq), 21 % over the four steps.

accomplished using ammonium formate and sodium cyanoborohydride to yield per-*O*-benzylated 1-deoxy-*melibio*-nojirimycin **8** (52 % yield, three steps). The chirality of carbon C5 of the piperidine moiety was unambiguously established by proton NMR, revealing that, as expected, the iminosugar moiety



Scheme 5. Reagents and conditions: a) TMSOTf, CH_2Cl_2, 0 °C, 69 %. b) 1) TBAF, THF; 2) *p*TsOH, CH_2Cl_2; 3) NaH, BnBr, DMF, 57 % over the three steps. c) 1) NIS, TFA, CH_2Cl_2; 2) $LiAlH_4$, THF; 3) oxalyl chloride, DMSO, Et_3N, –78 °C; 4) HCO_2NH_4, Na_2SO_4, $NaCNBH_3$; 5) H_2, Pd/C (10 %), DMF/MeOH, HCl (aq), 8 % over the five steps.

had 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 stereochemistry of **8**, 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[6c]). Removal of the benzyl groups in **8** by palladium-catalyzed hydrogenation gave the target imino-disaccharide **9** in 11 % overall yield starting from **1**.

The synthesis strategy applied for the assembly of 4-*O*-(α-D-glucopyranosyl)-1-deoxynojirimycin (**14**, 1-deoxy-*malto*-DNJ) was identical as described for the synthesis of **8**, starting from maltose (**10**).

Lactol **12** was uneventfully obtained from maltose **10** in a yield of 47 % over the five steps. Lithium aluminum hydride reduction of **12** followed by Swern oxidation (**12** to **13**) of both primary and secondary alcohol and double reductive amination produced fully protected 1-deoxy-*malto*-DNJ (33 % yield, three steps). The stereochemical outcome in synthesizing **32** was again demonstrated by proton NMR spectroscopy (see the Experimental Section). The benzyl groups were removed by palladium-catalyzed hydrogenolysis to form target iminosugar **14** in 11 % overall yield starting from **10**.

The synthesis of 4-*O*-(β-D-galactopyranosyl)-1-deoxynojirimycin **19** (1-deoxy-*lacto*-DNJ) starts with lactose **15** (Scheme 3), which is one of the cheapest disaccharide known and is a side product of the dairy industry. Peracetylation of lactose **15** followed by generation of the thiolactoside, Zémplen removal of the acetates, benzyl protection and NIS/TFA thioglycoside hydrolysis as described before afforded lactol **17**. In the next series of events, lactol **17** was reduced (lithium aluminum hydride), subjected to Swern oxidation (**17** to **18**) followed by a double reductive amination and treatment with palladium on carbon and dihydrogen gas to give the desired imino-disaccharide **19** in 14 % overall yield starting from **15**.

Starting from cellobiose **20**, 4-*O*-(β-D-glucopyranosyl)-1-deoxynojirimycin **24** (1-deoxy-*cellobio*-DNJ) was obtained (Scheme 4) in 10 % overall yield following the sequence of events as described for the synthesis of **9** (1-deoxy-*melobio*-DNJ).

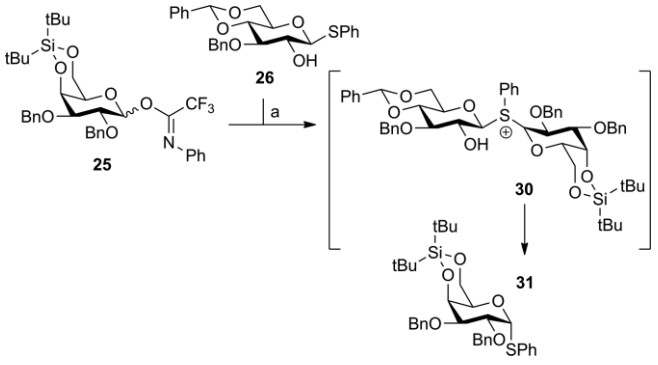
The examples described above (compounds **9**, **14**, **19** and **24**, Scheme 1, Scheme 2, Scheme 3, and Scheme 4) comprise the use of cheap, readily available disaccharides featuring a glucopyranose moiety at the reducing end as starting material. Obviously, many disaccharides other than the ones 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 is exemplified in Scheme 5.

Gal-DNJ [2-*O*-(α-D-galactopyranosyl)-1-deoxynojirimycin] **29** is one of several glycosylated DNJ derivatives (including 1-deoxy-*melobio*-DNJ, **24**) found both in mulberry trees (*Morus alba* L.) and silkworms (*Bombyx mori* L.) that feed on leaves from these trees, and is a moderately potent inhibitor of digestive glycosidases (maltase, sucrose) in rat.[2c] In order to access compound **29** following the general procedure subject of this work, the appropriately protected disaccharide **28** is required, which on paper can be derived from 2-*O*-(α-D-galactopyranosyl)-glucose. In contrast to other disaccharides, however, this disaccharide is scarce and not commercially available, and thus the route of synthesis as outlined in Scheme 5 is followed.

Treatment of the donor monosaccharide, *N*-phenyl-trifluoromethyl galactose imidate **25** (prepared following the literature procedures,[10] see the Experimental Section) and the acceptor monosaccharide, thioglycopyranoside **26** (see for its preparation[11] the Experimental Section) with trimethylsilyl trifluoromethanesulfonate in dichloromethane at 0 °C gave fully protected disaccharide **27** in 69 % yield and excellent α-stereoselectivity, as expected for glycosylations of 4–6-*O*-silylidene protected galactopyranose donors.[12] Sequential removal of the silylidene protective group (treatment with tetrabutyl ammonium fluoride) and the benzylidene protective group (treatment with catalytic *p*-toluenesulfonic acid) followed by benzylation of the thus liberated four hydroxyl groups afforded fully benzylated phenylthiodisaccharide **28**. This disaccharide was then transformed into Gal-DNJ **29** following the established sequence of events: thioacetal hydrolysis, hemiacetal reduction, oxidation of both primary and secondary alcohol, double reductive amination and final global debenzylation.

One interesting though not fully explained observation we made during our efforts to synthesize phenylthiodisaccharide **27** is that, when executing the glycosylation at –78 °C, the reaction turned out to be unproductive. Instead of obtaining **27**, no less than 70 % of α-phenylthiogalactoside **31** (Scheme 6) was obtained, with little to no formation of compound **27** observed. Elevating the reaction temperature appeared to favor formation of **27** over that of **31**. At –20 °C, the product ration of **27**:**31** was 35:30, and as described above, at 0 °C compound **27** was obtained as the exclusive isolated compound in good yield.

Although we have no satisfactory explanation for the temperature dependence of this aglycon transfer (See Scheme 6),



Scheme 6. Reagents and conditions: a) TMSOTf, CH_2Cl_2, –78 °C, 70 %.

there is literature precedence[13] for this phenomenon. This undesirable aglycon transfer is generally circumvented by the use of bulky anomeric thiols or tuning of the protecting groups of the acceptor, but these approaches require new synthetic routes to the acceptor nucleophile. Although the reasons for the shift in reaction outcome as a function of the reaction temperature remain unclear at present it does represent a very effective means to circumvent the unproductive side reaction.

In conclusion, this work reports on the synthesis of five glycosylated 1-deoxynojimycin derivatives. Four of these, namely 6-*O*-(α-D-galactopyranosyl)-1-deoxynojirimycin (**9**), 4-*O*-(α-D-glucopyranosyl)-1-deoxynojirimycin (**14**), 4-*O*-(β-D-glucopyranosyl)-1-deoxynojirimycin (**19**) and 4-*O*-(β-D-galactopyranosyl)-1-deoxynojirimycin (**24**) 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 (Gal-DNJ, **29**) 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 synthesis schemes glycosylated DNJ derivatives can be prepared without difficulties from their glycosylated glucose counterparts, as long as the latter are synthetically tractable. One intrinsic shortcoming of the presented procedure is the temporarily destruction of the chiral center at C5 (glucopyranose numbering). Whereas recovery in the presented examples of this chiral center during reductive amination is excellent, such stereoselectivity may not occur when starting from differently configured reducing sugars. Thus the presented methodology will likely be less fruitful when targeting disaccharidic iminosugars featuring, say, a mannojirimycin or galactonojirimycin iminosugar. On the positive side, L-*ido*-configured iminosugar disaccharides should be within easy reach by bismesylation of the diol in, for instance, **6** (Scheme 1), followed by nucleophilic displacement of both mesylates with an amine. Such a strategy would again transpose a route of synthesis that has been proven[6b] to be versatile for the construction of non-glycosylated iminosugars to tailored starting materials yielding glycosylated ones. Another obvious extension would be to start, not from disaccharides, but rather from oligosaccharides (for instance, cello/malto oligosaccharides) and thus prepare larger oligosaccharides, the reducing end sugar of which is substituted for DNJ.

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 with activated 4 Å molecular sieves for at least 12 hours before use. Compounds were visualized during TLC analyses by UV (254 nm), and with the staining solutions: aqueous solution of $KMnO_4$ (5 g/L) and K_2CO_3 (25 g/L). Visualization of hemi-acetals 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 NMR 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. 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 rotations 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 polymer 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 × 150 mm column).

1,2,3,4-Tetra-*O*-acetyl-6-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl)-β-glucopyranose (2): 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 ×), was added in small portions. The mixture was heated to reflux for 1 hour. TLC analysis confirmed complete consumption of the starting material **1** (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 × 150 mL) and brine (150 mL) and 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 **2** in 90 % yield (17.8 g, 26.2 mmol). R_F = 0.39 (1:1, PE/EtOAc). ^1H NMR (400 MHz, $CDCl_3$): δ/ppm = 5.70 (d, J = 8.3 Hz, 1 H, H-1), 5.45 (d, J = 2.9 Hz, 1 H, H-4′), 5.34 (dd, J = 10.8, 3.3 Hz, 1 H, H-3′), 5.27 (t, J = 9.4 Hz, 1 H, H-4), 5.16 (m, 2 H, H-1′, H-4), 5.07 (m, 2 H, H-2, H-3), 4.21 (dd, J = 11.4, 5.0 Hz, 1 H, H-5′), 4.15–4.02 (m, 3 H, H-2′, H-6), 3.83 (ddd, J = 9.9, 3.9, 2.6 Hz, 1 H, H-5), 3.74 (dd, J = 11.7, 4.3 Hz, 1 H, H-6′a), 3.65 (dd, J = 11.8, 2.3 Hz, 1 H, H-6′b), 2.24–1.96 (m, 24 H, 8 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 170.7–169.1 (C=O), 96.5 (C-1′), 91.7 (C-1), 73.6 (C-5), 73.0 (C-4), 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 × CH_3).

2,3,4-Tri-*O*-acetyl-6-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl)-1-thio-D-glucopyranose (3): PhSH (5.2 mL, 51.0 mmol) was added to a stirred solution of **2** (17.8 g, 26.2 mmol) in dry DCM (50 mL) and kept under argon atmosphere. After cooling the solution to 0 °C, BF_3·Et_2O (4.9 mL, 39.7 mmol) was added dropwise,

upon which the solution turned to orange. The mixture was stirred for 4 hours at room temperature, 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. $NaHCO_3$ (100 mL, 2 ×). The organic layer was dried (Na_2SO_4). After filtration, concentration and evaporation of the volatiles, the crude product was purified by silica gel column chromatography (3:1 → 7:3 → 1:1, PE/EtOAc), to give **3** as a 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/ppm = 7.45 (dd, J = 8.0, 1.4 Hz, 2 H, H_{Ar} SPh), 7.40–7.30 (m, 3 H, H_{Ar} SPh), 5.35 (dd, J = 3.5, 1.2 Hz, 1 H, H-4′), 5.32 (dd, J = 10.2, 3.4 Hz, 1 H, H-3′), 5.24 (t, J = 9.4 Hz, 1 H, H-3), 5.14 (d, J = 3.7 Hz, 1 H, H-1′), 5.11 (dd, J = 10.2, 3.7 Hz, 1 H, H-2′), 5.03 (t, J = 9.6 Hz, 1 H, H-4), 4.96 (dd, J = 10.1, 9.2 Hz, 1 H, H-2), 4.78 (d, J = 10.1 Hz, 1 H, H-1), 4.21 (td, J = 6.6, 1.3 Hz, 1 H, H-5′), 4.03 (d, J = 6.9 Hz, 2 H, H_2-6′), 3.77 (dd, J = 10.6, 5.8 Hz, 1 H, H-6b), 3.71 (dd, J = 5.8, 2.0 Hz, 1 H, H-5), 3.56 (dd, J = 10.7, 1.9 Hz, 1 H, H-6a), 2.15–1.99 (m, 21 H, 7 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 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 × CH_3). $[\alpha]_D^{20}$ = +73.3 (c = 1.14, $CHCl_3$). IR: $\tilde{\nu}$/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 (4): Compound **3** (15.0 g, 20.6 mmol) was co-evaporated with toluene (3 ×) and 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 more polar product. The mixture was diluted with MeOH after which Amberlite H^+ was added until the pH was adjusted to 7. After filtration and concentration the thus obtained product (D-galactopyranosyl-1-thio-D-glucopyranose) was co-evaporated with toluene (3 ×), dissolved in DMF (100 mL), and BnBr (20.9 mL, 176 mmol) was added. The solution was cooled to 0 °C, and 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 cooling down to 0 °C, the reaction mixture was quenched with MeOH, after which the volatiles were evaporated and EtOAc (200 mL) added. The mixture was washed with HCl solution (1 M, 100 mL, 2 ×). 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 **4** 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/ppm = 7.54–7.12 (m, 40 H, H_{Ar} SPh/Bn), 5.03 (d, J = 3.5 Hz, 1 H, H-1′), 4.66 (d, J = 9.9 Hz, 1 H, H-1), 4.97–4.37 (m, 14 H, 7 × CH_2 Bn), 4.05 (dd, J = 9.7, 3.5 Hz, 1 H, H-2′), 3.99 (t, J = 6.5 Hz, 1 H, H-5), 3.89 (m, 1 H, H-3′), 3.86 (d, J = 2.9 Hz, 1 H, H-4′), 3.78 (qd, J = 11.7, 3.5 Hz, 2 H, H_2-6′), 3.68–3.59 (m, 2 H, H-3, H-4), 3.54 (dd, J = 9.3, 5.9 Hz, 1 H, H-5′), 3.49 (dd, J = 9.5, 6.5 Hz, 2 H, H_2-6), 3.26 (dd, J = 9.9, 8.5 Hz, 1 H, H-2). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 139.0–138.1 (C_q Bn), 134.2 (C_q SPh), 131.9–127.5 (C_{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 × CH_2 Bn), 75.3 (C-3′), 75.1, 74.9, 73.4, 73.2, 72.8 (5 × CH_2 Bn), 72.8, 69.3 (C-5), 69.1 (C-6), 66.4 (C-6′). IR: $\tilde{\nu}$/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 (5): NIS (22 mg, 97 μmol) and TFA (30 μL, 0.39 μmol) were added to a cooled solution of **4** (94 mg, 88 μmol) in DCM (2 mL) at 0 °C. After an hour of stirring TLC analysis (4:1, toluene/EtOAc) showed complete consumption of the starting material. Sat. aq. $Na_2S_2O_3$ (7 mL) followed by sat. aq. $NaHCO_3$ (7 mL) were added. The mixture was diluted with DCM, and 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 **5** 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/ppm = 7.41–7.19 (m, 35 H, H_{Ar} Bn), 5.09 (d, J = 3.6 Hz, 1 H, H-1′), 4.98 (d, J = 3.5 Hz, 1 H, H-1), 4.95–4.28 (m, 14 H, 7 × CH_2 Bn), 4.13 (dt, J = 14.3, 6.8 Hz, 1 H, H-5′), 4.07–3.98 (m, 2 H, H-4, H-5), 3.96–3.88 (m, 3 H, H-2′, H-3, H-4′), 3.85 (d, J = 11.7 Hz, 1 H, H-6′b), 3.72 (dd, J = 12.0, 5.5 Hz, 1 H, H-6′b), 3.64–3.43 (m, 3 H, H-2, H-6), 3.39 (dd, J = 9.4, 3.5 Hz, 1 H, H-2), 3.26 (dd, J = 8.6, 7.3 Hz, 1 H, H-3′). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 138.9, 138.8, 138.4, 138.3, 138.1, 137.9, 137.8 (7 × C_q Bn), 128.6–127.6 (C_{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 × CH_2 Bn), 70.8 (C-5′), 69.6 (C-5), 69.6 (C-6), 67.8 (C-6′). $[\alpha]_D^{20}$ = +38.1 (c = 1.03, $CHCl_3$). IR: $\tilde{\nu}$/cm^{-1} = 3030, 2920, 2868, 2247, 1497, 1454, 1357, 1090, 1026. HRMS: found 995.4343 $[C_{61}H_{64}O_{11} + Na]^+$, calculated for $[C_{61}H_{64}O_{11} + Na]^+$ 995.4341.

2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-D-glucitol (6): $LiAlH_4$ in THF (6.0 mL, 2 M, 12.0 mmol) was slowly added to a cooled (0 °C) solution of **5** (3.91 g, 4.02 mmol, co-evaporated 3 × with toluene), in dry THF (40 mL) under argon atmosphere. The mixture was stirred overnight allowing the temperature to reach room temperature 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 with H_2O. Then NaOH solution (3 M, 40 mL) was added followed by celite. The solution was stirred until a homogeneous mixture was formed 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, after which the residue was purified by silica gel column chromatography (4:1 → 7:3 → 3:2, PE/EtOAc) to give **6** as a 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/ppm = 7.41–7.19 (m, 35 H, H_{Ar} Bn), 4.88 (d, J = 3.7 Hz, 1 H, H-1′), 5.03–4.29 (m, 14 H, CH_2 Bn), 4.06 (dd, J = 10.0, 3.6 Hz, 1 H, H-2′), 4.02–3.93 (m, 3 H, H-4′, H-5, H-5′), 3.92–3.86 (m, 2 H, H-3, H-3′), 3.82 (dd, J = 11.1, 5.3 Hz, 1 H, H-6a), 3.78–3.68 (m, 4 H, H-4, H-1a, H-2, H-4, H-6b), 3.55 (dd, J = 11.3, 4.3 Hz, 1 H, H-1b), 3.49 (d, J = 6.5 Hz, 2 H, H-6′). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 138.7–138.0 (C_q Bn), 128.6–127.5 (C_{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 × CH_2 Bn), 74.8 (C-4′), 73.9–72.9 (5 × CH_2 Bn), 70.6 (C-6), 70.4 (C-5′), 69.8 (C-5), 69.0 (C-6′), 61.9 (C-1). $[\alpha]_D^{20}$ = +34.4 (c = 1.02, $CHCl_3$). IR: $\tilde{\nu}$/cm^{-1} = 3335, 2974, 2289, 1636, 1456, 1418, 1088, 1045. HRMS: found 997.4491 $[C_{61}H_{64}O_{11} + Na]^+$, calculated for $[C_{61}H_{64}O_{11} + Na]^+$ 997.4497.

2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,4,6-tetra-α-D-galactopyranosyl)-1-deoxynojirimycin (8): 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 min, **7** (4.28 g, 3.22 mmol, co-evaporated 3 × with toluene), in dry DCM (18 mL), was added dropwise to the mixture. The reaction was stirred for 2 h 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 $NaCNBH_3$ (0.81 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 room temperature. 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. $NaHCO_3$ (200 mL). The organic layer was dried (Na_2SO_4), filtered and concentrated, and the crude product was purified with silica gel column chromatography (4:1 → 7:3 → 3:2 → 1:1, PE/EtOAc) to give the **8** in 71 % yield (2.17 g, 2.27 mmol). R_F = 0.4 (1:1, PE/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.45–7.16 (m, 35 H, H_{Ar} Bn), 4.91 (d, J = 3.7 Hz, 1 H, H-1′), 5.05–4.26 (m, 14 H, 7 × CH_2 Bn), 4.06 (dd, J = 10.0, 3.6 Hz, 1 H, H-2′), 3.97 (d, J = 2.7 Hz, 1 H, H-4′), 3.98–3.93 (m, 2 H, H-3′, H-5′), 3.86 (dd, J = 10.5, 5.3 Hz, 1 H, H-6a), 3.64 (dd, J = 10.5, 2.6 Hz, 1 H, H-6b), 3.54 (dd, J = 9.1, 2.5 Hz, 1 H, H-6′a), 3.53 (t, J = 9.0 Hz, 1 H, H-3), 3.49 (dd, J = 9.3, 6.1 Hz, 1 H, H-6′b), 3.32 (t, J = 9.2 Hz, 1 H, H-2), 3.31 (t, J = 9.5, 1 H, H-4), 2.95 (dd, J = 12.5, 5.1, 1 H, H-1′a), 2.68 (ddd, J = 9.6, 5.2, 2.6, 1 H, H-5), 2.37 (dd, J = 12.4, 10.7, 1 H, H-1′b). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 138.8–137.9 (C_q Bn), 128.4–127.4 (C_{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 × CH_2 Bn), 74.7 (C-4′), 73.6, 73.4, 72.6, 72.6 (4 × CH_2 Bn), 69.6 (C-5′), 69.4 (C-6), 68.8 (C-6′), 59.5 (C-5), 47.7 (C-1). IR: $\tilde{\nu}$/cm^{-1} = 3032, 2899, 2872, 1497, 1453, 1354, 1208, 1093, 1059, 1027. $[\alpha]_D^{20}$ = +58.2 (c = 0.5, $CHCl_3$). HRMS: found 956.4736 $[C_{61}H_{66}NO_9 + H]^+$, calculated for $[C_{61}H_{66}NO_9 + H]^+$ 956.4732.

6-*O*-(α-D-Galactopyranosyl)-1-deoxynojirimycin (9): A mixture of DMF/MeOH (1:1, 20 mL), HCl (2 mL, 1 M) and **8** (2.00 g, 2.09 mmol) was flushed with argon (3 ×). Then a catalytic amount of Pd/C (20 %) was added, after which H_2 was flushed through the mixture, letting the solution shake overnight under H_2 atmosphere (4 bar). HPLC analysis showed complete conversion of starting material into 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 ×) with MilliQ water, product **9** was obtained as a white solid in 75 % yield (326 mg, 1.00 mmol). ^{1}H NMR (400 MHz, MeOD): δ/ppm = 4.84 (d, J = 3.4 Hz, 1 H, H-1′), 4.01 (dd, J = 10.5, 4.7 Hz, 1 H, H-6a), 3.90 (dd, J = 3.0, 1.2 Hz, 1 H, H-4′), 3.84 (td, J = 6.1, 1.1 Hz, 1 H, H-5′), 3.80 (dd, J = 10.1, 3.4 Hz, 1 H, H-2′), 3.76 (dd, J = 10.1, 3.0 Hz, 1 H, H-3′), 3.70 (d, J = 6.1 Hz, 2 H, H-6′), 3.59 (dd, J = 10.4, 2.5 Hz, 1 H, H-6b), 3.52 (ddd, J = 11.0, 9.1, 5.1 Hz, 1 H, H-2), 3.38 (dd, J = 10.1, 9.0, 1 H, H-4), 3.25 (t, J = 9.0 Hz, 1 H, H-3), 3.20 (dd, J = 12.3, 5.1 Hz, 1 H, H-1a), 2.82 (ddd, J = 10.0, 4.6, 2.6 Hz, 1 H, H-5), 2.60 (dd, J = 12.3, 11.0 Hz, 1 H, H-1b). ^{13}C NMR (100 MHz, MeOD): δ/ppm = 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). $[\alpha]_D^{20}$ = +92.8 (c = 1.0, MeOH). IR: $\tilde{\nu}$/cm^{-1} = 3482, 2928, 2962, 1653, 1506, 1409, 1437, 1387, 1255, 1092, 1063. HRMS: found 326.1446 $[C_{12}H_{23}NO_9M + H]^+$, calculated for $[C_{12}H_{23}NO_9 + H]^+$ 326.1446.

1,2,3,6-Tetra-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-β-glucopyranose (11): A suspension of Ac_2O (59.0 mL, 0.625 mol) and NaOAc (4.33 g, 52.8 mmol) were heated to reflux. When refluxing began the heat source was removed and maltose (9.94 g, 29.0 mmol, co-evaporated with 3 × toluene) 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) and 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 × 150 mL) and brine (200 mL). After the organic layer was dried (Na_2SO_4), filtered, and concentrated, the residue was purified by silica gel column chromatography (1:1 → 1:2 → 0:1, PE/EtOAc) to give pure **11** in 94 % yield (18.5 g, 27.3 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 5.74 (d, J = 8.2 Hz, 1 H, H-1), 5.42 (dd, J = 12.4, 4.0 Hz, 1 H, H-1′), 5.36 (dd, J = 9.8, 2.3 Hz, 1 H, H-3), 5.33–5.26 (m, 1 H, H-3′), 5.11–4.94 (m, 2 H, H-4′, H-2), 4.86 (ddd, J = 10.5, 6.2, 4.0 Hz, 1 H, H-2′), 4.45 (dd, J = 12.3, 2.4 Hz, 1 H, H-6′a), 4.27–4.19 (m, 2 H, H-6a, H-6′b), 4.14–4.08 (m, 1 H, H-6b), 4.04 (ddd, J = 8.9, 5.8, 3.8 Hz, 1 H, H-4), 3.96–3.91 (m, 1 H, H-5′), 3.84 (ddd, J = 9.6, 4.3, 2.5 Hz, 1 H, H-5), 2.26–1.96 (m, 24 H, 8 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 170.6–168.9 (8 × 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 × CH_3).

2,3,6-Tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-α/β-glucopyranose (12): Step 1: According to the procedure described for the preparation for compound **3**, 1,2,3,6-tetra-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-β-glucopyranose (12.1 g, 16.5 mmol, 61 % yield) was synthesized from **11** (18.5 g, 27.3 mmol) as a colorless oil. R_F = 0.43 (1:1, PE/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.51–7.44 (m, 2 H, H_{Ar} SPh), 7.36–7.28 (m, 3 H, H_{Ar} SPh), 5.39 (d, J = 4.0 Hz, 1 H, H-1′), 5.34 (dd, J = 10.5, 9.6 Hz, 1 H, H-3), 5.28 (t, J = 8.9 Hz, 1 H, H-3′), 5.04 (t, J = 9.9 Hz, 1 H, H-4′), 4.85 (dd, J = 10.5, 4.0 Hz, 1 H, H-2′), 4.79 (d, J = 9.0 Hz, 1 H, H-2), 4.73 (d, J = 10.1 Hz, 1 H, H-1), 4.54 (dd, J = 12.1, 2.5 Hz, 1 H, H-6′a), 4.24 (dd, J = 10.5, 4.5 Hz, 1 H, H-6a), 4.21 (dd, J = 10.2, 4.4 Hz, 1 H, H-6′b), 4.04 (dd, J = 10.2, 4.4 Hz, 1 H, H-6b), 3.95 (dd, J = 9.7, 9.0 Hz, 1 H, H-4), 3.94 (ddd, J = 10.4, 4.0, 2.4 Hz, 1 H, H-5′), 3.72 (ddd, J = 9.8, 4.8, 2.6 Hz, 1 H, H-5), 2.14–1.99 (m, 21 H, 7 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 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 (7 × CH_3). $[\alpha]_D^{20}$ = +30.6 (c = 1.0, $CHCl_3$). IR: $\tilde{\nu}$/cm^{-1} = 1746, 1368, 1223, 1038, 912. **Step 2:** According to the procedure described for the preparation for compound **4**, 2,3,6-tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-1-thio-D-glucopyranose (15.4 g, 14.5 mmol, 89 % yield) was synthesized from the above mentioned acetyl phenylthiomaltoside (11.9 g, 13.3 mmol) as a light yellow oil. R_F = 0.63 (4:1, PE/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.60 (dd, J = 6.5, 3.0 Hz, 2 H, H_{Ar} SPh), 7.33–7.16 (m, 32 H, H_{Ar} Bn, H_{Ar} SPh), 7.13–7.08 (m, 6 H, H_{Ar} Bn), 5.64 (d, J = 3.6 Hz, 1 H, H-1′), 4.92–4.76 (m, 6 H, 3 × CH_2 Bn), 4.70 (d, J = 9.7 Hz, 1 H, H-1), 4.62–4.41 (m, 7 H, 7 × CH*H*Bn), 4.31 (d, J = 12.1 Hz, 1 H, CH*H*Bn), 4.12 (t, J = 9.2 Hz, 1 H, H-4), 3.93 (dd, J = 9.9, 8.9 Hz, 1 H, H-3′), 3.89 (dd, J = 11.3, 4.3 Hz, 1 H, H-6′a), 3.83 (dd, J = 6.5, 4.3 Hz, 1 H, H-6′b), 3.82 (t, J = 8.8 Hz, 1 H, H-3), 3.79 (dd, J = 7.3, 2.7 Hz, 1 H, H-5′), 3.67 (dd, J = 17.1, 8.0 Hz, 1 H, H-4′), 3.60 (dd, J = 11.2, 1.8 Hz, 1 H, H-6a), 3.59 (dd, J = 10.5, 3.3 Hz, 1 H, H-5), 3.58 (t, J = 10.2 Hz, 1 H, H-2), 3.51 (dd, J = 9.9, 3.7 Hz, 1 H, H-2′), 3.45 (dd, J = 10.6, 1.8 Hz, 1 H, H-6b). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 138.7–137.8 (7 × 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 × CH_2Bn), 72.7 (C-4), 71.1 (C-5′), 69.2 (C-6′), 68.3 (C-6). $[\alpha]_D^{20}$ = +2.87 (c = 2.31, $CHCl_3$). IR: $\tilde{\nu}$/cm^{-1} = 3063, 3030, 2904, 2864, 1452, 1360, 1207, 1140, 1084, 1055, 1026. **Step 3:** Compound **12** (12.3 g, 12.3 mmol, 93 % yield) was synthesized from 2,3,6-tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-1-thio-*d*-glucopyranose (14.5 g, 13.6 mmol) according to the procedure described for the preparation for compound **5**, 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/ppm = 7.31–7.07 (m, 35 H, H_{Ar} Bn), 5.66 (dd, J = 8.6, 3.6 Hz, 1 H, H-1′), 5.21 (t, J = 2.9 Hz, 1 H, H-1), 5.02–4.26 (m, 14 H, 7 × CH_2 Bn), 4.31 (dd, J = 12.2, 10.0 Hz, 1 H, H-4), 4.13 (t, J = 8.8 Hz, 1 H, H-3), 4.03–3.82 (m, 2 H, H-3′, H-5), 3.80–3.58 (m, 5 H, H-2, H-4′, H-5′, H_2-6′), 3.55–3.45 (m, 2 H, H-2′, H-6a), 3.39 (ddd, J = 10.7, 3.6, 1.7 Hz, 1 H, H-6b). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 138.9, 138.7, 138.4, 138.2, 138.0, 137.9, 137.7 (7 × C_q Bn), 128.4 127.1 (C_{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 × CH_2 Bn), 72.9 (C-3), 71.1 (C-5), 69.6 (C-5′), 69.2 (C-6′), 68.1 (C-6). $[\alpha]_D^{20}$ = +32.8 (c = 1.0, $CHCl_3$). IR: $\tilde{\nu}$/cm^{-1} =

3418, 3063, 3030, 2903, 2864, 1497, 1452, 1362, 1265, 1207, 1146, 1088, 1043, 1026.

4-*O*-(α-D-Glucopyranosyl)-1-deoxynojirimycin (14): Step 1: According to the procedure described for the preparation for compound **6**, 2,3,6-Tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-D-glucitol (8.33 g, 8.55 mmol, 74 % yield) was synthesized from **12** (11.25 g, 11.57 mmol) as a light yellow oil. R_F = 0.31 (7:3, PE/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.36–7.07 (m, 35 H, H_{Ar} Bn), 4.82 (d, *J* = 3.1 Hz, 1 H, H-1′), 4.96–4.35 (m, 14 H, 7 × CH_2 Bn), 4.12 (dd, *J* = 8.6, 4.0 Hz, 1 H, H-3′), 3.98 (ddd, *J* = 10.2, 3.2, 2.1 Hz, 1 H, H-5), 3.96–3.90 (m, 4 H, H-5′, H-4, H-3′, H-4′), 3.78–3.64 (m, 2 H, H_2-1), 3.60–3.53 (m, 6 H, H_2-6, H_2-6′, H-2, H-2′). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 138.2–137.6 (C_q Bn), 129.1–125.4 (C_{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 × CH_2 Bn), 71.8 (C-3′), 71.6 (C-6), 71.2 (C-5), 68.3 (C-6′), 61.6 (C-1). $[\alpha]_D^{20}$ = +38.1 (*c* = 1.03, $CHCl_3$). IR: ṽ/cm^{-1} = 3420, 3063, 3030, 2862, 1454, 1207, 1086, 1070, 1028. HRMS: found 997.4497 $[C_{61}H_{64}O_{11} + H]^+$, calculated for $[C_{61}H_{64}O_{11} + Na]^+$ 997.4497. **Step 2:** According to the procedure described for the preparation for compound **8**, 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-1-deoxynojirimycin (0.428 g, 0.448 mmol, 44 % yield) was synthesized from 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-D-glucitol (0.998 g, 1.02 mmol) as a light yellow oil. R_F = 0.38 (1:1, PE/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.49–7.26 (m, 35 H, H_{Ar} Bn), 5.94 (d, *J* = 3.6 Hz, 1 H, H-1′), 5.30–4.46 (m, 14 H, 7 × CH_2 Bn), 4.11 (dd, *J* = 9.8, 8.5 Hz, 1 H, H-3′), 3.98 (dd, *J* = 9.5, 8.7 Hz, 1 H, H-4), 3.93–3.87 (m, 2 H, H-5′, H-6a), 3.88 (t, *J* = 8.7 Hz, 1 H, H-3), 3.84 (dd, *J* = 8.7, 1.3 Hz, 1 H, H-4′), 3.81 (dd, *J* = 8.7, 5.6 Hz, 1 H, H-6b), 3.73 (dd, *J* = 10.6, 2.8 Hz, 1 H, H-6′a), 3.73–3.70 (m, 1 H, H-2), 3.67 (dd, *J* = 9.8, 3.6 Hz, 1 H, H-2′), 3.61 (dd, *J* = 10.4, 1.3 Hz, 1 H, H-6′b), 3.42 (dd, *J* = 12.3, 5.1 Hz, 1 H, H-1a), 3.03 (ddd, *J* = 9.1, 5.8, 2.9, 1 H, H-5), 2.70 (dd, *J* = 12.3, 10.6 Hz, 1 H, H-1b). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 139.1–137.9 (7 × C_q Bn), 128.3–126.5 (C_{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 × CH_2 Bn), 74.2 (C-4), 73.8–72.5 (5 × CH_2 Bn), 71.0 (C-5′), 70.5 (C-6), 68.1 (C-6′), 59.0 (C-5), 47.8 (C-1). $[\alpha]_D^{20}$ = +26.0 (*c* = 0.7, $CHCl_3$). IR: ṽ/cm^{-1} = 2918, 2866, 1454, 1362, 1240, 1090, 1072, 1047, 1026. HRMS: found 956.4731 $[C_{61}H_{66}NO_9 + H]^+$, calculated for $[C_{61}H_{66}NO_9 + H]^+$ 956.4732. **Step 3:** Compound **14** (0.24 g, 0.74 mmol, 71 % yield) was synthesized from 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-1-deoxynojirimycin (1.00 g, 1.04 mmol) according to the procedure described for the preparation for compound **9**, as a light yellow oil. ^{1}H NMR (400 MHz, MeOD): δ/ppm = 5.21 (d, *J* = 3.7 Hz, 1 H, H-1′), 4.00 (dd, *J* = 12.1, 4.8 Hz, 1 H, H-6a), 3.91 (dd, *J* = 12.0, 3.0 Hz, 1 H, H-6b), 3.88–3.83 (m, 1 H, H-6′a), 3.77 (ddd, *J* = 4.8, 8.9, 10.8 Hz, 1 H, H-2). 3.81–3.66 (m, 4 H, H-3′, H-4′, H-6′b, H-3), 3.62 (dd, *J* = 9.7, 9.0 Hz, 1 H, H-4) 3.49 (dd, *J* = 9.7, 3.8 Hz, 1 H, H-2′), 3.35 (dd, *J* = 12.5, 5.0 Hz, 1 H, H-1a), 3.30–3.23 (m, 2 H, H-5′, H-5), 2.91 (dd, *J* = 12.4, 10.9 Hz, 1 H, H-1b). ^{13}C NMR (100 MHz, MeOD): δ/ppm = 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). $[\alpha]_D^{20}$ = +25.0 (*c* = 0.2, MeOH). IR: ṽ/cm^{-1} = 3303, 2967, 1636, 1560, 1203, 1161, 1022. HRMS: found 326.1446 $[C_{12}H_{23}NO_9 + H]^+$, calculated for $[C_{12}H_{23}NO_9 + H]^+$ 326.1446.

2,3,6-Tri-*O*-benzyl-4-(2′,3′,4′,6′-tetra-*O*-benzyl-β-D-galactopyranosyl)-α/β-D-glucopyranose (17): Step 1: According to the procedure described for the preparation for compound **4**, 2,3,6-tri-*O*-benzyl-4-(2′,3′,4′,6′-tetra-*O*-benzyl-β-D-galactopyranosyl)-1-thio-D-glucopyranose (5.32 g, 5.00 mmol, 100 % yield) was synthesized from lactose (3.64 g, 5.00 mmol) as a light yellow oil. R_F = 0.67 (4:1, PE/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.61–7.04 (m, 40 H, H_{Ar} Bn/SPh), 4.67 (d, *J* = 10.5 Hz, 1 H, H-1), 5.13–4.20 (m, 14 H, CH_2 Bn), 4.45 (d, *J* = 7.7 Hz, 1 H, H-1′), 4.00–3.91 (m, 2 H, H-4′, H-5′), 3.82 (dd, *J* = 11.0, 4.3 Hz, 1 H, H-6′a), 3.79–3.73 (m, 2 H, H-2′, H-6′b), 3.61 (t, *J* = 8.9 Hz, 1 H, H-3′), 3.52 (t, *J* = 7.6 Hz, 1 H, H-6a), 3.47–3.31 (m, 5 H, H-2, H-3, H-4, H-5 H-6b). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 139.2–138.2 (7 × C_q Bn), 133.8 (C_q SPh), 132.2–127.3 (C_{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 × CH_2 Bn), 73.7 (C-5′), 73.5, 73.2 (2 × CH_2 Bn), 73.1 (C-5), 72.2 (CH_2 Bn), 68.5 (C-6′), 68.2 (C-6). IR: ṽ/cm^{-1} = 3030, 2920, 2862, 1497, 1454, 1362, 1209, 1088, 1076, 1028, 1001. **Step 2:** Compound **17** (96.0 mg, 98.7 μmol, 85 % yield) was synthesized from 2,3,6-tri-*O*-benzyl-4-(2′,3′,4′,6′-tetra-*O*-benzyl-β-D-galactopyranosyl)-1-thio-D-glucopyranose (0.12 g, 0.12 mmol) according to the procedure described for the preparation for compound **5**, as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.61–7.04 (m, 40 H, H_{Ar} Bn/SPh), 5.16 (d, *J* = 3.7 Hz, 1 H, H-1), 5.10–4.17 (m, 14 H, CH_2 Bn), 4.33 (d, *J* = 9.4 Hz, 1 H, H-1′), 3.99–3.87 (m, 3 H, H-2′, H-3′, H-5′), 3.87–3.80 (m, 2 H, H-4, H-3), 3.74 (ddd, *J* = 10.0, 7.5, 2.4 Hz, 1 H, H-6′a), 3.65 (dd, *J* = 10.5, 1.6 Hz, 1 H, H-6′b), 3.52 (ddd, *J* = 12.7, 9.3, 6.7 Hz, 2 H, H-2, H-6a), 3.42–3.29 (m, 4 H, H-3, H-4′, H-5, H-6b). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 139.3–138.1 (C_q Bn), 128.5–127.2 (C_{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 × CH_2 Bn), 75.1 (C-4′), 74.8 (CH_2 Bn), 73.8 (C-4), 73.7, 73.6, 73.2 (3 × CH_2 Bn), 73.2 (C-5′), 72.7 (CH_2 Bn), 70.5 (C-5), 68.3 (C-6′), 68.1 (C-6). $[\alpha]_D^{20}$ = +12.4 (*c* = 1.07, $CHCl_3$). IR: ṽ/cm^{-1} = 2920, 2864, 1452, 1396, 1362, 1207, 1090. HRMS: found 995.4342 $[C_{61}H_{64}O_{11} + Na]^+$, calculated for $[C_{61}H_{64}O_{11} + Na]^+$ 995.4341.

4-(β-D-Galactopyranosyl)-1-deoxynojirimycin (19): Step 1: According to the procedure described for the preparation for compound **6**, 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-D-glucitol (4.17 g, 4.28 mmol, 77 % yield) was synthesized from **17** (5.44 g, 5.59 mmol) as a light yellow oil. R_F = 0.20 (7:3, PE/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.36–7.18 (m, 35 H, H_{Ar} Bn), 4.97–4.22 (m, 14 H, 7 × CH_2 Bn), 4.34 (dd, *J* = 7.2, 5.4 Hz, 1 H, H-1′), 4.03 (dd, *J* = 7.4, 2.4 Hz, 1 H, H-4), 3.99 (dt, *J* = 7.9, 3.8 Hz, 2 H, H-2, H-5′), 3.95 (dd, *J* = 7.8, 2.4 Hz, 1 H, H-3), 3.83 (d, *J* = 2.9 Hz, 1 H, H-4′), 3.77 (dd, *J* = 9.8, 7.7 Hz, 1 H, H-2′), 3.71 (dd, *J* = 6.9, 3.7, 2 H, H_2-1), 3.66 (dd, *J* = 9.9, 4.4 Hz, 1 H, H-6′a), 3.55 (dd, *J* = 9.8, 3.0 Hz, 1 H, H-6′b), 3.48 (dd, *J* = 6.3, 2.5 Hz, 2 H, H_2-6), 3.42 (dd, *J* = 10.0, 6.4 Hz, 1 H, H-5), 3.40 (dd, *J* = 9.7, 3.0 Hz, 1 H, H-3′). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 138.8–137.7 (C_q Bn), 128.5 (C_{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 × CH_2 Bn), 73.8 (C-4′), 73.6, 73.3 (2 × CH_2 Bn), 73.3 (C-5), 73.2, 73.0 (2 × CH_2 Bn), 70.8 (C-5′), 70.8 (C-6′), 68.9 (C-6), 62.3 (C-1). IR: ṽ/cm^{-1} = 3028, 2922, 2864, 1063, 1026, 1001. $[\alpha]_D^{20}$ = +6.6 (*c* = 1.0, $CHCl_3$). HRMS: found 997.4498 $[C_{61}H_{66}O_{11} + Na]^+$, calculated for $[C_{61}H_{66}O_{11} + Na]^+$ 997.4497. **Step 2:** According to the procedure described for the preparation for compound **8**, 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-1-deoxynojirimycin (0.90 g, 0.94 mmol, % yield) was synthesized from 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-D-glucitol (4.17 g, 4.28 mmol) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.45–7.09 (m, 35 H, H_{Ar} Bn), 4.95 (d, *J* = 11.6 Hz, 1 H CH*H* Bn), 4.83 (d, *J* = 11.6 Hz, 2 H, CH_2 Bn), 4.85 (d, *J* = 11.4 Hz, 1 H, CH*H* Bn), 4.75 (d, *J* = 11.9 Hz, 1 H, CH*H* Bn), 4.71 (d, *J* = 11.6 Hz, 2 H, CH_2 Bn), 4.67 (d, *J* = 11.5 Hz, 1 H, CH*H* Bn), 4.57 (d, *J* = 11.7 Hz, 1 H, CH*H* Bn), 4.44 (d, *J* = 11.7 Hz, 1 H, CH_2 Bn), 4.38 (d, *J* = 11.8 Hz, 1 H, CH*H* Bn), 4.35 (d, *J* = 11.7 Hz, 1 H, CH*H* Bn), 4.34 (d, *J* = 7.7 Hz, 1 H, H-1′), 4.30 (d, *J* = 11.9 Hz, 1 H, CH*H* Bn), 4.05 (dd, *J* = 7.8, 2.4 Hz, 1 H, H-4), 4.01 (dd, *J* = 7.6, 3.7 Hz, 1 H, H-5′), 4.00 (d, *J* = 3.4 Hz, 1 H, H-2),3.96 (dd, *J* = 7.8, 2.4 Hz, 1 H, H-3), 3.85 (d, *J* = 2.9 Hz, 1 H, H-4′), 3.79 (dd, *J* = 9.7, 7.7 Hz, 1 H, H-2′), 3.73 (dd, *J* = 8.6, 3.4 Hz, 2 H, H_2-1), 3.68 (dd, *J* = 10.0, 4.2 Hz, 1 H,

H-6′a), 3.57 (dd, *J* = 9.8, 3.0 Hz, 1 H, H-6′b), 3.50 (dd, *J* = 6.3, 1.5 Hz, 2 H, H_2-6), 3.44 (d, *J* = 5.8 Hz, 1 H, H-5), 3.42 (dd, *J* = 9.8, 2.9 Hz, 1 H, H-3′). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 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 × CH_2 Bn), 73.7 (C-3), 73.6 (CH_2 Bn), 73.3 (C-5), 73.3–72.9 (3 × CH_2 Bn), 70.8 (C-2), 70.8 (C-6′), 68.9 (C-6), 62.3 (C-1). IR: $\tilde{\nu}$/cm^{-1} = 3060, 3029, 2916, 2866, 1497, 1453, 1361, 1208, 1097, 1028. $[\alpha]_D^{20}$ = +14.0 (*c* = 0.4, $CHCl_3$). HRMS: found 956.4734 $[C_{61}H_{66}O_9N + Na]^+$, calculated for $[C_{61}H_{66}O_9N + H]^+$ 956.4732. **Step 3: 19** (0.20 g, 0.621 mmol, 64 % yield) was synthesized from 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-1-deoxynojirimycin (0.932 g, 0.975 mmol) according to the procedure described for the preparation for compound **9**, as a light yellow oil. ^{1}H NMR (400 MHz, MeOD): δ/ppm = 4.44 (d, *J* = 7.6 Hz, 1 H, H-1′), 3.92 (d, *J* = 3.7 Hz, 2 H, H_2-6), 3.92 (d, *J* = 3.2, 1.1 Hz, 1 H, H-4′), 3.87 (dd, *J* = 11.4, 7.4 Hz, 1 H, H-6′a), 3.79 (dd, *J* = 11.4, 4.7 Hz, 1 H, H-6′b), 3.67 (ddd, *J* = 7.4, 4.7, 1.1 Hz, 1 H, H-5′), 3.65 (dd, *J* = 9.8, 7.6 Hz, 1 H, H-2′), 3.58 (dd, *J* = 9.7, 3.3 Hz, 1 H, H-3′), 3.55 (ddd, *J* = 5.1, 9.1, 10.7 Hz, 1 H, H-2), 3.50 (dd, *J* = 9.5, 8.8 Hz, 1 H, H-4), 3.44 (t, *J* = 8.7 Hz, 1 H, H-3), 3.17 (dd, *J* = 12.4, 5.1 Hz, 1 H, H-1a), 2.71 (dt, *J* = 9.6, 3.8 Hz, 1 H, H-5), 2.54 (dd, *J* = 12.5, 10.7 Hz, 1 H, H-1b). ^{13}C NMR (100 MHz, MeOD): δ/ppm = 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). $[\alpha]_D^{20}$ = +16.0 (*c* = 0.2, MeOH). IR: $\tilde{\nu}$/cm^{-1} = 3306, 2945, 2833, 1653, 1448, 1410, 1113, 1018. HRMS: found 326.1448 $[C_{12}H_{23}NO_9 + Na]^+$, calculated for $[C_{12}H_{23}NO_9 + H]^+$ 326.1446.

2,3,6-Tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-1-thio-D-glucopyranose (21): Compound **21** (19.5 g, 28.8 mmol, 98 % yield) was synthesized from D-(+)-cellobiose **20** (10.0 g, 29.2 mmol) according to the procedure described for the preparation for compound **2**. R_F = 0.36 (1:1, PE/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 5.66 (d, *J* = 8.2 Hz, 1 H, H-1), 5.23 (t, *J* = 9.2 Hz, 1 H, H-3′), 5.18–4.99 (m, 3 H, H-3, H-4, H-2), 4.97–4.87 (m, 1 H, H-2′), 4.52–4.47 (m, 2 H, H-6′a, H-1′), 4.37 (dd, *J* = 12.3, 4.4 Hz, 1 H, H-6a), 4.12 (dd, *J* = 12.2, 4.6 Hz, 1 H, H-6′b), 4.05 (dd, *J* = 12.5, 2.1 Hz, 1 H, H-6b), 3.82 (dd, *J* = 15.6, 6.5 Hz, 1 H, H-4′), 3.75 (ddd, *J* = 9.8, 4.7, 1.8 Hz, 1 H, H-5), 3.66 (ddd, *J* = 9.9, 4.4, 2.4 Hz, 1 H, H-5′). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 170.6–169.0 (8 × 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 × CH_3).

2,3,6-Tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-α/β-glucopyranose (22): Step 1: According to the procedure described for the preparation for compound 3, 2,3,6-tri-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-1-thio-D-glucopyranose (0.67 g, 0.91 mmol, 91 % yield) was synthesized from **21** (0.68 g, 1.00 mmol), as a colorless oil. R_F = 0.53 (1:1, PE/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 5.20 (dd, *J* = 10.4, 8.0 Hz, 1 H, H-3′), 5.15 (dd, *J* = 9.4, 7.2 Hz, 1 H, H-3), 5.06 (t, *J* = 9.7 Hz, 1 H, H-4), 4.91 (ddd, *J* = 10.0, 8.6, 3.7 Hz, 2 H, H-2, H-2′), 4.70 (d, *J* = 10.1 Hz, 1 H, H-1′), 4.56 (dd, *J* = 11.9, 2.0 Hz, 1 H, H-6′a), 4.54 (d, *J* = 7.9 Hz, 1 H, H-1), 4.38 (dd, *J* = 12.5, 4.3 Hz, 1 H, H-6a), 4.11 (td, *J* = 7.1, 1.9 Hz, 1 H, H-6′b), 4.03 (dd, *J* = 12.4, 2.0 Hz, 1 H, H-6b), 3.75 (m, 1 H, H-4′), 3.69 (ddd, *J* = 8.9, 3.9, 1.8 Hz, 1 H, H-5), 3.65 (dd, *J* = 5.7, 2.0 Hz, 1 H, H-5′). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 170.3–168.8 (7 × 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 × CH_3). $[\alpha]_D^{20}$ = +30.6 (*c* = 1.0, $CHCl_3$). IR: $\tilde{\nu}$/cm^{-1} = 2958, 2872, 1743, 1440, 1368, 1216, 1168, 1038. HRMS: found 751.1878 $[C_{32}H_{40}O_{17}S + Na]^+$, calculated for $[C_{32}H_{40}O_{17}S + Na]^+$ 751.1878. **Step 2:** According to the procedure described for the preparation for compound **4**, 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-1-thio-D-glucopyranose (15.4 g, 14.5 mmol, 89 % yield) was synthesized from the 2,3,6-tri-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-1-thio-D-glucopyranose (11.9 g, 13.3 mmol) as a light yellow oil. R_F = 0.63 (4:1, PE/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.60 (dd, *J* = 6.5, 3.0 Hz, 2 H, H_{Ar} SPh), 7.33–7.16 (m, 32 H, H_{Ar} Bn, H_{Ar} SPh), 7.13–7.08 (m, 6 H, H_{Ar} Bn), 5.64 (d, *J* = 3.6 Hz, 1 H, H-1′), 4.92–4.76 (m, 6 H, CH_2 Bn), 4.70 (d, *J* = 9.7 Hz, 1 H, H-1), 4.62–4.41 (m, 7 H, CH_2 Bn), 4.31 (d, *J* = 12.1 Hz, 1 H, CH_2 Bn), 4.12 (t, *J* = 9.2 Hz, 1 H, H-4), 3.93 (dd, *J* = 9.9, 8.9 Hz, 1 H, H-3′), 3.89 (dd, *J* = 11.3, 4.3 Hz, 1 H, H-6a′), 3.83 (dd, *J* = 6.5, 4.3 Hz, 1 H, H-6b′), 3.82 (t, *J* = 8.8 Hz, 1 H, H-3), 3.79 (dd, *J* = 7.3, 2.7 Hz, 1 H, H-5′), 3.67 (dd, *J* = 17.1, 8.0 Hz, 1 H, H-4′), 3.60 (dd, *J* = 11.2, 1.8 Hz, 1 H, H-6a), 3.59 (dd, *J* = 10.5, 3.3 Hz, 1 H, H-5), 3.58 (t, *J* = 10.2 Hz, 1 H, H-2), 3.51 (dd, *J* = 9.9, 3.7 Hz, 1 H, H-2′), 3.45 (dd, *J* = 10.6, 1.8 Hz, 1 H, H-6b). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 138.7–137.8 (7 × 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 × CH_2 Bn), 72.7 (C-4), 71.1 (C-5′), 69.2 (C-6′), 68.3 (C-6). $[\alpha]_D^{20}$ = +2.87 (*c* = 2.31, $CHCl_3$). IR: $\tilde{\nu}$/cm^{-1} = 3063, 3030, 2904, 2864, 1452, 1360, 1207, 1140, 1084, 1055, 1026. HRMS: found 1087.4429 $[C_{61}H_{64}O_{11} + Na]^+$, calculated for $[C_{61}H_{64}O_{11} + Na]^+$ 1087.4425. **Step 3:** 22 (12.3 g, 12.3 mmol, 93 % yield) was synthesized from 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-1-thio-D-glucopyranose (14.5 g, 13.6 mmol) according to the procedure described for the preparation for compound 5, 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/ppm = 7.31–7.07 (m, 35 H, H_{Ar} Bn), 5.66 (dd, *J* = 8.6, 3.6 Hz, 1 H, H-1′), 5.21 (t, *J* = 2.9 Hz, 1 H, H-1), 5.02–4.26 (m, 14 H, 7 × CH_2 Bn), 4.31 (dd, *J* = 12.2, 10.0 Hz, 1 H, H-4), 4.13 (t, *J* = 8.8 Hz, 1 H, H-3), 4.03–3.82 (m, 2 H, H-3′, H-5), 3.80–3.58 (m, 5 H, H-2, H-4′, H-5′, H-6′), 3.55–3.45 (m, 2 H, H-2′, H-6a), 3.39 (ddd, *J* = 10.7, 3.6, 1.7 Hz, 1 H, H-6b). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 138.9–137.7 (7 × C_q Bn), 128.4–127.1 (C_{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 × CH_2 Bn), 72.9 (C-3), 71.1 (C-5), 69.6 (C-5′), 69.2 (C-6′), 68.1 (C-6). $[\alpha]_D^{20}$ = +32.8 (*c* = 1.0, $CHCl_3$). IR: $\tilde{\nu}$/cm^{-1} = 3418, 3063, 3030, 2903, 2864, 1497, 1452, 1362, 1265, 1207, 1146, 1088, 1043, 1026. HRMS: found 995.4339 $[C_{61}H_{64}O_{11} + Na]^+$, calculated for $[C_{61}H_{64}O_{11} + Na]^+$ 995.4341.

4-*O*-(β-D-Glucopyranosyl)-1-deoxynojirimycin (24): Step 1: According to the procedure described for the preparation for compound **6**, 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-D-glucitol (8.33 g, 8.55 mmol, 74 % yield) was synthesized from **22** (11.2 g, 11.6 mmol) as a light yellow oil. R_F = 0.31 (7:3, PE/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.36–7.07 (m, 35 H, H_{Ar} Bn), 4.82 (d, *J* = 3.1 Hz, 1 H, H-1′), 4.96–4.35 (m, 14 H, 7 × CH_2 Bn), 4.12 (dd, *J* = 8.6, 4.0 Hz, 1 H, H-3′), 3.98 (ddd, *J* = 10.2, 3.2, 2.1 Hz, 1 H, H-5), 3.96–3.90 (m, 4 H, H-5′, H-4, H-3′, H-4′), 3.71 (dt, *J* = 29.8, 6.9 Hz, 2 H, H-1), 3.52–3.62 (m, 6 H, H_2-6, H_2-6′, H-2, H-2′). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 138.2–137.6 (7 × C_q Bn), 129.1–125.4 (C_{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 × CH_2 Ph), 71.8 (C-3′), 71.6 (C-6), 71.2 (C-5), 68.3 (C-6′), 61.6 (C-1). IR: $\tilde{\nu}$/cm^{-1} = 3420, 3063, 3030, 2862, 1454, 1207, 1086, 1070, 1028. $[\alpha]_D^{20}$ = +38.1 (*c* = 1.03, $CHCl_3$). HRMS: found 997.4497 $[C_{61}H_{66}O_{11} + Na]^+$, calculated for $[C_{61}H_{66}O_{11} + Na]^+$ 997.4497. **Step 2:** According to the procedure described for the preparation for compound **8**, 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)-1-deoxynojirimycin (0.43 g, 0.45 mmol, 44 % yield) was synthesized from 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-D-glucitol (1.0 g, 1.02 mmol) as a light yellow oil. R_F = 0.38 (1:1 PE, EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.49–7.26 (m, 35 H, H_{Ar} Bn), 5.94 (d, *J* =

3.6 Hz, 1 H, H-1′), 5.30–4.46 (m, 14 H, 7 × CH_2 Bn), 4.11 (dd, *J* = 9.8, 8.5 Hz, 1 H, H-3′), 3.98 (dd, *J* = 9.6, 8.7 Hz, 1 H, H-4), 3.93–3.87 (m, 3 H, H-5′, H-6a, H-3), 3.84 (dd, *J* = 8.7, 1.3 Hz, 1 H, H-4′), 3.81 (dd, *J* = 8.7, 5.6 Hz, 1 H, H-6b), 3.73 (dd, *J* = 10.6, 2.8 Hz, 1 H, H-6a′), 3.72 (td, *J* = 5.3, 2.2 Hz, 1 H, H-2), 3.67 (dd, *J* = 9.8, 3.6 Hz, 1 H, H-2′), 3.61 (dd, *J* = 10.4, 1.3 Hz, 1 H, H-6b′), 3.42 (dd, *J* = 12.3, 5.1 Hz, 1 H, H-1a), 3.03 (ddd, *J* = 9.0, 5.7, 2.8, 1 H, H-5), 2.70 (dd, *J* = 12.3, 10.6 Hz, 1 H, H-1b). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 139.1–137.9 (7 × C_q Bn), 128.3–126.5 (C_{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 × CH_2 Bn), 74.2 (C-4), 73.8–72.5 (5 × CH_2 Ph), 71.0 (C-5′), 70.5 (C-6), 68.1 (C-6′), 59.0 (C-5), 47.8 (C-1). $[\alpha]_D^{20}$ = +26.0 (*c* = 0.7, $CHCl_3$). IR: $\tilde{\nu}$/cm^{-1} = 2918, 2866, 1454, 1362, 1240, 1090, 1072, 1047, 1026. HRMS: found 956.4736 $[C_{61}H_{66}NO_9 + Na]^+$, calculated for $[C_{61}H_{66}NO_9 + Na]^+$ 956.4732. **Step 3:** Compound **24** (0.22 g, 0.67 mmol, 65 % yield) was synthesized from 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl)-1-deoxynojirimycin (1.00 g, 1.04 mmol) according to the procedure described for the preparation for compound **8**, as a light yellow oil. ^{1}H NMR (600 MHz, D_2O): δ/ppm = 4.46 (d, *J* = 7.9 Hz, 1 H, H-1′), 3.88 (dd, *J* = 12.3, 3.1 Hz, 1 H, H-6a), 3.84 (dd, *J* = 12.4, 2.2 Hz, 1 H, H-6′a), 3.66 (dd, *J* = 12.4, 5.7 Hz, 1 H, H-6′b), 3.66–3.62 (m, 1 H, H-2), 3.62 (dd, *J* = 10.4, 8.9 Hz, H-5′), 3.49 (t, *J* = 9.1 Hz, 1 H, H-3), 3.42 (q, *J* = 9.5 Hz, 1 H, H-3′), 3.42–3.39 (m, 1 H, 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, 1 H, H-5), 2.70 (dd, *J* = 12.5, 11.2 Hz, 1 H, H-1b). ^{13}C NMR (150 MHz, D_2O): δ/ppm = 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). $[\alpha]_D^{20}$ = +25.3 (*c* = 1.0, MeOH). IR: $\tilde{\nu}$/cm^{-1} = 3302, 2966, 1636, 1558, 1203, 1161, 1022. HRMS: found 326.1446 $[C_{12}H_{23}NO_9 + H]^+$, calculated for $[C_{12}H_{23}NO_9 + H]^+$ 326.1446.

Phenyl-3-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (26): The glucose acceptor was prepared following the literature procedures.[11] **Step 1:** β-D-Glucose penta-acetate (1.00 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•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), filtered and concentrated. The crude product was purified with silica gel column chromatography to gain the phenyl-1-thio-2,3,4,6-tetra-(*O*-acetyl)-β-D-glucopyranoside as white crystals (1.02 g, 2.33 mmol, yield 91 %). R_F = 0.7 (5:3, PE/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.55–7.49 (m, 2 H, H_{Ar} SPh), 7.34 (dd, *J* = 5.1, 2.0 Hz, 3 H, H_{Ar} SPh), 5.24 (t, *J* = 9.3 Hz, 1 H, H-3), 5.06 (t, *J* = 9.8 Hz, 1 H, H-4), 4.99 (dd, *J* = 10.1, 9.2 Hz, 1 H, H-2), 4.73 (d, *J* = 10.1 Hz, 1 H, H-1), 4.24 (dd, *J* = 12.3, 5.0 Hz, 1 H, H-6a), 4.20 (dd, *J* = 12.3, 2.7 Hz, 1 H, H-6b), 3.75 (ddd, *J* = 10.1, 5.0, 2.7 Hz, 1 H, H-5), 2.11 (s, 3 H, CH_3), 2.10 (s, 3 H, CH_3), 2.04 (s, 3 H, CH_3), 2.01 (s, 3 H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 170.6, 170.2, 169.4, 169.3 (4 × 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 × CH_3). **Step 2:** NaOMe (0.28 g, 5.12 mmol) was added to a solution of the phenyl-1-thio-2,3,4,6-tetra-(*O*-acetyl)-β-D-glucopyranoside (2.56 mmol) in MeOH (20 mL). After 24 hours, TLC analysis showed complete consumption. The solution was neutralized with amberlite H^+ resin, filtered and concentrated. The crude deprotection 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/ppm = 7.60–7.57 (m, 2 H, H_{Ar} SPh), 7.35–7.26 (m, 3 H, H_{Ar} SPh), 4.63 (d, *J* = 9.6 Hz, 1 H, H-1), 3.91 (dd, *J* = 12.4, 1.6 Hz, 1 H, H-6a), 3.71 (dd, *J* = 12.0, 5.6, 1 H, H-6b), 3.43 (t, *J* = 8.8, 1 H, H-4), 3.37–3.29 (m, 2 H, H-3, H-5), 3.26 (dd, *J* = 9.6, 8.8, 1 H, H-2). ^{13}C NMR (100 MHz, MeOD): δ/ppm = 133.8 (C_q Ph), 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). **Step 3:** $PhCH(OMe)_2$ (5.70 mL, 38 mmol) was added to the solution of phenyl-1-thio-β-D-glucopyranoside (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 reduced to 20 mbar. After 4.5 hours, TLC analysis showed complete consumption. 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 with warm ethanol to get pure 4,6-*O*-benzylidene thioglucopyranoside as 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/ppm = 7.58–7.55 (m, 2 H, H_{Ar} Ph), 7.59–7.57 (m, 3 H, H_{Ar} Ph), 7.41–7.37 (m, 5 H, H_{Ar} Ph), 5.57 (s, 1 H, H-7), 4.69 (d, *J* = 9.6 Hz, 1 H, H-1), 4.44 (dd, *J* = 10.4, 4.4 Hz, 1 H, H-6a) 3.91 (t, *J* = 8.8 Hz, 1 H, H-3) 3.85 (dd, *J* = 7.2 Hz, 3.2 Hz, 1 H, H-6b), 3.51–3.55 (m, 2 H, H-4, H-5), 3.53 (dd, *J* = 11.8, 8.4 Hz, 1 H, H-2). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 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). **Step 4:** Bu_2SnO (0.35 g, 1.40 mmol) was added to a solution of 4,6-*O*-benzylidene thioglucopyranoside (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, the reaction mixture was diluted with EtOAc, 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 **26** (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/ppm = 5.60 (s, 1 H, C_t *H* Ph), 4.99 (d, *J* = 11.5 Hz, 1 H, CH*H* Bn), 4.83 (d, *J* = 11.6 Hz, 1 H, CH*H* Bn), 4.67 (d, *J* = 9.7 Hz, 1 H, H-1), 4.42 (dd, *J* = 10.5, 5.0 Hz, 1 H, H-6), 3.83 (t, *J* = 10.3 Hz, 1 H, H-6), 3.76–3.63 (m, 2 H, H-3, H-4), 3.58–3.53 (m, 2 H, H-2, H-5). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 138.2, 137.2 (C_q Ph), 133.2–126.0 (C_{Ar} Ph), 101.3 (C-7), 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).

2,3-Di-*O*-benzoyl-4,6-*O*-di-*tert*-butylsilanediyl-D-galactopyranoside-*N*-phenyl-2,2,2-trifluoroacetimidate (25): The galactose imidate is prepared following the literature procedures.[10] **Step 1:** Phenyl-1-thio-2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (1.2 g, 2.5 mmol, 100 %) was synthesized from β-D-galactose pentaacetate (1.00 g, 2.56 mmol), thiophenol (0.4 mL, 3.91 mmol) and BF_3•Et_2O (0.46 mL, 3.72 mmol) according to the procedure described for the preparation of the phenyl-1-thio-2,3,4,6-tetra-(*O*-acetyl)-β-D-glucopyranoside, as white crystal. R_F = 0.68 (5:3, PE/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.52–7.52 (m, 2 H, H_{Ar}), 7.34–7.32 (m, 3 H, H_{Ar}), 5.44 (d, *J* = 3.2, 1 H, H-1), 5.28 (t, *J* = 10 Hz, 1 H, H-2), 5.08 (dd, *J* = 10, 3.6 Hz, 1 H, H-3), 4.75 (d, *J* = 10.0 Hz, 1 H, H-4), 4.23 (dd, *J* = 11.2, 7.2 Hz, 1 H, H-6a), 4.15 (dd, *J* = 11.6, 6 Hz, 1 H, H-6b), 3.98 (t, *J* = 6.4 Hz, 1 H, H-5), 2.14 (s, 3 H, CH_3), 2.11 (s, 3 H, CH_3), 2.06 (s, 3 H, CH_3), 1.99 (s, 3 H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 170.4–169.5 (4 × 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). **Step 2:** Phenyl-1-thio-β-D-galactopyranoside was synthesized from the phenyl-1-thio-2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (59.00 g, 133.95 mmol), using thiophenol (0.4 mL, 3.91 mmol) and BF_3•Et_2O (0.46 mL, 3.72 mmol) according to the procedure described for the deprotection of the phenyl-1-thio-β-D-glucopyranoside. The crude product was used in next step without further purification. The crude thiogalactopyranoside (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 the starting compound. MeOH was added to quench the reaction. The solution was concentrated and diluted with EtOAc, washed with HCl (1 M) and sat. aq. $NaHCO_3$. The organic layer was dried (Na_2SO_4), filtered and concentrated. The residue was purified with silica gel column chromatography (1:4 → 1:3, EtOAc/PE) to gain the 4,6-*O*-di-*tert*-butylsilylene thiogalactopyranoside (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/ppm = 7.62–7.52 (m, 2 H, H_{Ar}), 7.39–7.30 (m, 3 H, H_{Ar}), 4.58 (d, *J* = 9.8 Hz, 1 H, H-1), 4.46 (dd, *J* = 3.5, 1.1 Hz, 1 H, H-4), 4.29 (dd, *J* = 2.0, 1.1 Hz, 2 H, H-6), 3.77 (dd, *J* = 9.8, 8.9 Hz, 1 H, H-2), 3.56 (dd, *J* = 8.9, 3.5 Hz, 1 H, H-3), 3.50 (td, *J* = 2.0, 1.1 Hz, 1 H, H-5), 1.08 (s, 9 H, 3 × CH_3), 1.06 (s, 9 H, 3 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 133.1 (C_q), 132.6–127.9 (CH_{Ar}), 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 × CH_3, *tert*-Bu). **Step 3:** 4,6-*O*-di-*tert*-butylsilylene thiogalactopyranoside (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. The mixture was quenched with water, diluted with EtOAc and washed with brine. The organic layer was dried (Na_2SO_4), filtered and concentrated. The residue was purified with silica gel column chromatography (20:1 → 10:1, PE/EtOAc) to gain 2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene thiogalactopyranoside (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/ppm = 7.61–7.27 (m, 12 H, H_{Ar}), 4.94 (s, 2 H, CH_2 Bn), 4.80 (q, *J* = 18.8 Hz, 12 Hz, 2 H, CH_2 Bn), 4.71 (d, *J* = 9.6 Hz, 1 H, H-1), 4.53 (d, *J* = 2.8 Hz, 1 H, H-4), 4.24 (m, 2 H, H-6), 3.89 (t, *J* = 9.6 Hz, 1 H, H-2), 3.52 (dd, *J* = 9.2, 3.2 Hz, 1 H, H-3), 3.32 (s, 1 H, H-5), 1.17(s, 9 H, *tert*-Bu), 1.12 (s, 9 H, *tert*-Bu). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 138.4, 134.9 (C_q), 132.1–127.3 (C_{Ar}), 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). **Step 4:** 2,3-Di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene thiogalactopyranoside (0.61 g, 1.0 mmol, co-evaporated 3 × with toluene) was dissolved in DCM (50 mL). The solution was cooled to 0 °C. *N*-Iodosuccinimide (0.23 g, 1.03 mmol) and TFA (77 µL, 1.0 mmol) were added to the solution. After 1 hour, TLC analysis showed complete consumption. The reaction was quenched with TEA and sat. aq. $Na_2S_2O_3$ solution was added to the mixture. The mixture was extracted with EtOAc, and the organic layer was dried (Na_2SO_4), filtered and concentrated. The resulting residue was purified with silica gel column chromatography (10:1 → 2:1, PE/EtOAc) to gain the 2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-D-galactopyranoside (0.451 g, 0.903 mmol, yield 88 %). R_F = 0.28 (toluene). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.37–7.29 (m, 10 H, H_{Ar} Bn), 5.23 (d, *J* = 3.6 Hz, 1 H, H-1), 4.92 (d, *J* = 11.6 Hz, 2 H, C*H*$_2$ Bn), 4.81–4.72 (m, 2 H, C*H*$_2$ Bn), 4.54 (d, *J* = 3.0 Hz, 1 H, H-4), 4.21–4.12 (m, 2 H, H-6), 4.02 (dd, *J* = 9.6, 3.6 Hz, 1 H, H-2), 3.87 (d, *J* = 3.2 Hz, 1 H, H-5), 3.84 (d, *J* = 2.8 Hz, 1 H, H-3), 1.12, 1.08 (s, 9 H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 138.9, 138.3 (C_q Bn), 128.4–127.6 (C_{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). **Step 5:** 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 the 2,3-di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylene-D-galactopyranoside (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 filtered through a pad of celite to get rid of the Cs salt. The filtrate was concentrated and purified on a short column (20:1 → 2:1, PE/EtOAc) to obtain **25** (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/ppm = 7.52–6.78 (m, 15 H, H_{Ar} Bn), 6.55 (br-s, 1 H, H-1), 4.89 (d, *J* = 11.8 Hz, 1 H, CH*H* Bn), 4.85–4.72 (m, 3 H, 3 × CH*H* Bn), 4.62 (br-s, 1 H, H-4), 4.33–4.18 (m, 3 H, H-6, H-2), 3.91 (d, *J* = 10.1 Hz, 1 H, H-3), 3.81 (br-s, 1 H, H-5), 1.10 (s, 9 H, 3 × CH_3), 1.02 (s, 9 H, 3 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 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, *t*Bu).

3-Benzyl-4,6-*O*-benzylidene-2-*O*-(2,3-di-benzyl-4,6-*O*-di-*tert*-butylsilyl-galactopyranpsyl)-1-thio-D-glucopyranose (27): Compounds **26** (0.40 g, 0.90 mmol) and **25** (1.20 g, 1.79 mmol, co-evaporated 3 × with toluene). The mixture was dissolved in dried DCM (4 mL) and cooled to 0 °C, followed by adding of trimethylsilyl trifluoromethanesulfonate (0.045 mL, 0.25 mmol) dropwise. After an overnight reaction, TLC analysis showed complete consumption of **25**. The reaction was quenched with 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/ppm = 7.70–7.04 (m, 25 H, H_{Ar}), 5.89 (d, *J* = 4 Hz, 1 H, H-1′), 5.65 (s, 1 H, H-7), 5.09 (d, *J* = 10 Hz, 1 H, CH*H* Bn), 4.97 (d, *J* = 9.2 Hz, 1 H, H-1), 4.89 (s, 2 H, CH_2 Bn), 4.81 (q, *J* = 12, 13.5 Hz, 2 H, CH_2 Bn), 4.43 (dd, *J* = 10.8, 5.2 Hz, 1 H, H-6a), 4.33 (d, *J* = 10.4 Hz, 1 H, CH*H* Bn), 4.07 (dd, *J* = 10.0, 3.6 Hz, 1 H, H-2′), 4.02 (d, 8.0 Hz, 1 H, H-4′), 3.89–3.72 (m, 6 H, H-3, H-2, H-5′, H-6b, H-3′, H-4), 3.56 (dd, *J* = 12.8, 1.6 Hz, 1 H, H-6′a), 3.60–3.53 (m, 1 H, H-5), 3.02 (dd, *J* = 12.6, 2.2 Hz, 1 H, H-6′b), 1.02 (s, 9 H, 3 × CH_3), 0.99 (s, 9 H, 3 × CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 139.5–126.0 (C_{Ar}), 101.1 (C-7), 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). $[\alpha]_D^{20}$ = +34.0 (*c* = 2.60, $CHCl_3$). IR: $\tilde{\nu}$/cm^{-1} = 2933, 2858, 1735, 1473, 1453, 1440, 1373, 1241, 1170, 1149, 1097, 1044, 1025. HRMS: found 933.4068 $[C_{54}H_{64}O_{10}SSi + H]^+$, calculated for $[C_{54}H_{64}O_{10}SSi + H]^+$ 933.4068.

Phenyl-1-thio-2-*O*-(2,3,4,6-tetra-*O*-benzyl-α-galactopyranosyl)-3,4,6-tri-benzyl-D-glucopyranose (28): Step 1: TBAF (1 M *in* THF, 1.2 mL, 1.2 mmol) was added dropwise to a solution of **27** (0.16 g, 0.17 mmol) in THF (2 mL) at 0 °C, and the yellow solution was kept stirred at room temperature overnight. The reaction mixture was then diluted with EtOAc, washed with brine, dried (Na_2SO_4) filtered concentrated and the residue was purified with a silica gel column chromatography (5:2 → 1:1, PE/EtOAc) to get the 3-benzyl-4,6-*O*-benzylidene-2-*O*-(2,3-di-benzyl-galactopyranpsyl)-1-thio-D-glucopyranose (0.11 g, 0.14 mmol, yield 82 %). R_F = 0.17 (5:2, PE/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.52–7.17 (m, 25 H, H_{Ar}), 6.01 (d, *J* = 3.8 Hz, 1 H, H-1′), 5.63 (s, 1 H, H-7), 5.10 (d, *J* = 10.7 Hz, 1 H, CH*H* Bn), 4.96 (d, *J* = 9.3 Hz, 1 H, H-1), 4.87 (d, *J* = 11.7 Hz, 1 H, CH*H* Bn), 4.84 (d, *J* = 11.6 Hz, 1 H, CH*H* Bn), 4.77 (d, *J* = 11.7 Hz, 1 H, CH*H* Bn), 4.71 (d, *J* = 11.6 Hz, 1 H, CH*H* Bn), 4.48 (d, *J* = 10.7 Hz, 1 H, CH*H* Bn), 4.41 (dd, *J* = 10.5, 5.0 Hz, 1 H, H-6a), 4.06 (t, *J* = 4.8 Hz, 1 H, H-5′), 3.96–3.90 (m, 3 H, H-2, H-2′, H-3), 3.84 (d, *J* = 10.2 Hz, 1 H, H-6b), 3.81–3.78 (m, 1 H, H-4), 3.75 (dd, *J* = 10.0, 3.2 Hz, 1 H, H-3′), 3.59 (dd, *J* = 3.2, 1.5 Hz, 1 H, H-4′), 3.55 (dt, *J* = 9.8, 4.8 Hz, 1 H, H-5), 3.30 (dd, *J* = 11.8, 5.4 Hz, 1 H, H-6′a), 3.23 (dd, *J* = 11.8, 4.3 Hz, 1 H, H-6′b). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 137.9–125.9 (C_{Ar}), 101.1 (C-7), 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′). $[\alpha]_D^{20}$ = +22.1

(c = 0.85, $CHCl_3$). IR: $\tilde{\nu}/cm^{-1}$ = 3061, 2894, 1497, 1453, 1371, 1266, 1219, 1148, 1099, 1017. HRMS: found 815.2860 $[C_{46}H_{48}O_{10}S + Na]^+$, calculated for $[C_{46}H_{48}O_{10}S + Na]^+$ 815.2860. **Step 2:** *p*-Toluenesulfonic acid monohydrate (0.065 g, 0.34 mmol) was added to a solution of the 3-benzyl-4,6-*O*-benzylidene-2-*O*-(2,3-di-benzyl-galactopyranpsyl)-1-thio-D-glucopyranose (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 quenched with TEA, the reaction mixture was concentrated and purify with silica gel column chromatography (1:1, pentane/EtOAc) to gain phenyl-1-thio-2-*O*-(2,3-di-*O*-benzyl-α-galactopyranosyl)-3-benzyl-D-glucopyranose (0.08 g, yield 90 %). R_F = 0.1 (1:1, PE/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.53–7.16 (m, 15 H, H_{Ar}), 5.97 (d, J = 3.7 Hz, 1 H, H-1′), 5.06 (d, J = 11.2 Hz, 1 H, CH*H* Bn), 4.91 (d, J = 9.7 Hz, 1 H, H-1), 4.87 (d, J = 11.7 Hz, 1 H, CH*H* Bn), 4.82 (d, J = 11.8 Hz, 1 H, CH*H* Bn), 4.76 (d, J = 11.8 Hz, 1 H, CH*H* Bn), 4.71 (d, J = 11.7 Hz, 1 H, CH*H* Bn), 4.58 (d, J = 11.2 Hz, 1 H, CH*H* Bn), 4.05 (td, J = 5.2, 4.7, 2.3 Hz, 1 H, H-5′), 3.93 (dd, J = 10.1, 3.9 Hz, 1 H, H-2′), 3.90–3.79 (m, 4 H, H-6a, H-2, H-6b, H-3), 3.76 (dd, J = 10.0, 3.2 Hz, 1 H, H-3′), 3.66 (t, J = 9.0 Hz, 1 H, H-4), 3.54 (d, J = 2.9 Hz, 1 H, H-4′), 3.42–3.34 (m, 2 H, H-6′a, H-5), 3.26 (dd, J = 11.8, 4.0 Hz, 1 H, H-6′b). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 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). $[\alpha]_D^{20}$ = +16.3 (c = 2.45, $CHCl_3$). IR: $\tilde{\nu}/cm^{-1}$ = 3432, 3031, 2923, 1584, 1497, 1454, 1275, 1094, 1028. HRMS: found 727.2542 $[C_{39}H_{44}O_{10} + Na]^+$, calculated for $[C_{39}H_{44}O_{10} + Na]^+$ 727.2547. **Step 3:** NaH (60 % on mineral oil, 48.8 mg, 1.22 mmol) was added to a solution of phenyl-1-thio-2-*O*-(2,3-di-*O*-benzyl-α-galactopyranosyl)-3-benzyl-D-glucopyranose (0.08 g, 0.11 mmol) in 1 mL of DMF at 0 °C under argon atmosphere, the suspension was kept stirring 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 quenching with 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 **28** (0.11 g, 0.10 mmol, yield 92 %). R_F = 0.62 (5:1, PE/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.59–7.09 (m, 40 H, H_{Ar}), 6.01 (d, J = 3.7 Hz, 1 H, H-1′), 4.98 (d, J = 11.6 Hz, 1 H, CH*H* Bn), 4.92–4.53 (m, 10 H, 5 × CH_2 Bn), 4.49 (d, J = 11.4 Hz, 1 H, CH*H* Bn), 4.33 (t, J = 6.5 Hz, 1 H, H-5′), 4.30 (d, J = 12.0 Hz, 1 H, CH*H* Bn), 4.22 (d, J = 11.8 Hz, 1 H, CH*H* Bn), 4.12 (dd, J = 10.2, 3.6 Hz, 1 H, H-2′), 3.97 (t, J = 9.1 Hz, 1 H, H-2), 3.89 (dd, J = 10.2, 2.7 Hz, 1 H, H-3′), 3.81–3.72 (m, 3 H, H-6a, H-6b, H-4), 3.65 (t, J = 9.3 Hz, 1 H, H-3), 3.60 (dd, J = 2.9, 1.3 Hz, 1 H, H-4′), 3.55 (ddd, J = 9.8, 4.5, 2.1 Hz, 1 H, H-5), 3.44 (dd, J = 9.5, 6.4 Hz, 1 H, H-6′a), 3.28–3.23 (m, 1 H, H-6′b). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 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). $[\alpha]_D^{20}$ = +20.6 (c = 0.80, $CHCl_3$). HRMS: found 1087.4430 $[C_{67}H_{68}O_{10}S + Na]^+$, calculated for $[C_{67}H_{68}O_{10}S + Na]^+$ 1087.4431.

2-*O*-(α-D-Galactopyranosyl)-1-deoxynojirimycin (29): Step 1: NIS (0.13 g, 0.53 mmol) and TFA (35 μL) was added to a solution of **28** (0.44 g, 0.41 mmol) in dried DCM (5 mL) at 0 °C under argon atmosphere. The reaction was then kept 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 then diluted with EtOAc, washed with HCl solution (1 M) 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 2-*O*-(2,3,4,6-Tetra-*O*-benzyl-α-galactopyranosyl)-3,4,6-tri-*O*-benzyl-D-glucopyranose (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/ppm = 5.34 (d, J = 3.4 Hz, 1 H, H-1′), 4.99–4.50 (m, 13 H, 6 × CH_2 Bn, H-1), 4.41–4.28 (m, 2 H, CH_2 Bn), 4.15 (d, J = 7.2 Hz, 1 H, H-5), 4.12–4.05 (m, 2 H, H-5′, H-2), 4.00–3.89 (m, 3 H, H-4, H-4′, H-3′), 3.85 (dd, J = 9.0, 3.4 Hz, 1 H, H-2′), 3.83–3.70 (m, 3 H, H-6′, H-3), 3.49–3.45 (m, 2 H, H-6). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 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 × CH_2 Bn), 70.9 (C-5′), 69.7 (C-5), 68.6 (C-6′), 68.5 (C-6). $[\alpha]_D^{20}$ = +36.7 (c = 1.90, $CHCl_3$). IR: $\tilde{\nu}/cm^{-1}$ = 3027, 2901, 1724, 1497, 1453, 1364, 1263, 1208, 1067. HRMS: found 995.4343 $[C_{61}H_{64}O_{11} + Na]^+$, calculated for $[C_{61}H_{64}O_{11} + Na]^+$ 995.4341. **Step 2:** $LiAlH_4$ (0.5 mL, 2.4 M in THF, 1.2 mmol) was added dropwise into a solution of 2-*O*-(2,3,4,6-tetra-*O*-benzyl-α-galactopyranosyl)-3,4,6-tri-*O*-benzyl-D-glucopyranose (0.25 g, 0.26 mmol) in THF (3 mL) at 0 °C under argon atmosphere. After stirring overnight, the reaction mixture was slowly quenched with methanol, after which HCl (1 M, 3 mL) was added. Then the mixture was diluted with EtOAc and washed with brine, the water layer was extracted with EtOAc. The organic layer 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 2-*O*-(2,3,4,6-tetra-*O*-benzyl-α-galactopyranosyl)-3,4,6-tri-*O*-benzyl-D-glucitol (0.22 g, 0.23 mmol, yield 88 %). R_F = 0.58 (1:1, PE/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 5.05 (d, J = 3.5 Hz, 1 H, H-1′), 4.96–4.86 (m, 2 H, CH_2 Bn), 4.79–4.51 (m, 6 H, 3 × CH_2 Bn), 4.45 (d, J = 12.0 Hz, 1 H, CH*H* Bn), 4.35 (d, J = 12.0 Hz, 1 H, CH*H* Bn), 4.14–4.04 (m, 2 H, H-2, H-5′), 4.11 (dd, J = 10.1, 3.7 Hz, 1 H, H-2′), 4.00–3.98 (m, 1 H, H-5), 3.98 (dd, J = 10.1, 2.6 Hz, 1 H, H-3′) 3.92–3.82 (m, 3 H, H-3, H-4′, H-4), 3.81–3.76 (m, 1 H, H-6a), 3.76–3.71 (m, 2 H, H-6′), 3.69–3.64 (m, 1 H, H-6b), 3.52 (dd, J = 9.3, 6.7 Hz, 1 H, H-1a), 3.38 (dd, J = 9.4, 5.8 Hz, 1 H, H-1b). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 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 × CH_2 Bn), 71.2 (C-6′), 70.7 (C-5′), 70.4 (C-2), 69.4 (C-1), 62.5 (C-6). $[\alpha]_D^{20}$ = +39.1 (c = 1.17, $CHCl_3$). IR: $\tilde{\nu}/cm^{-1}$ = 3448, 3063, 3029, 2922, 2863, 1724, 1497, 1453, 1359, 1271, 1208, 1076, 1027. HRMS: found 997.4499 $[C_{61}H_{66}O_{11} + Na]^+$, calculated for $[C_{61}H_{66}O_{11} + Na]^+$ 997.4497. **Step 3:** 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 min 2-*O*-(2,3,4,6-Tetra-*O*-benzyl-α-galactopyranosyl)-3,4,6-tri-*O*-benzyl-D-glucitol (0.32 g, 0.33 mmol, co-evaporated 3 × with toluene), 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 1 h, 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 filtering, the solvents were evaporated, as the residue was dissolved in EtOAc (100 mL). The solution was washed with sat. aq. $NaHCO_3$ solution. The organic layer was dried (Na_2SO_4) filtered and concentrated. The residue was purified with silica gel column chromatography (5:1 → 2:3, PE/EtOAc) to give 2-*O*-(2,3,4,6-tetra-*O*-benzyl-α-galactopyranosyl)-3,4,6-tri-*O*-benzyl-1-deoxynojirimycin 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/ppm = 4.95–4.80 (m, 7 H, H-1′, 3 × CH_2 Bn), 4.72 (d, J = 11.8 Hz, 1 H, CH*H* Bn), 4.67 (d, J = 12.1 Hz, 1 H, CH*H* Bn), 4.57–4.44 (m, 4 H,

2 × CH_2 Bn), 4.31 (d, J = 6.2 Hz, 2 H, CH_2 Bn), 4.20 (td, J = 6.5, 1.3 Hz, 1 H, H-5′), 4.05 (dd, J = 10.1, 3.6 Hz, 1 H, H-2′), 3.89 (dd, J = 10.1, 2.9 Hz, 1 H, H-3′), 3.75 (dd, J = 9.2, 4.6 Hz, 1 H, H-2), 3.72–3.69 (m, 2 H, H-6a, H-4′), 3.65–3.59 (m, 1 H, H-6b), 3.60 (t, J = 9.2 Hz, 1 H, H-3), 3.52 (dd, J = 9.6, 6.4 Hz, 1 H, H-6′a), 3.41 (t, J = 9.3 Hz, 1 H, H-4), 3.32 (dd, J = 9.6, 6.6 Hz, 1 H, H-6′b), 3.25 (dd, J = 12.5, 4.8 Hz, 1 H, H-1e), 2.76 (ddd, J = 9.3, 5.0, 2.6 Hz, 1 H, H-5), 2.56 (dd, J = 12.5, 10.4 Hz, 1 H, H-1a). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 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 Ph), 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 × CH_2 Bn), 69.8 (C-6), 68.9 (C-6′), 68.8 (C-5′), 59.7 (C-5), 46.5 (C-1). $[\alpha]_D^{20}$ = +76.9 (c = 0.32, $CHCl_3$). IR: $\tilde{\nu}$/cm^{-1} = 2990, 2901, 1453, 1394, 1241, 1066, 1057, 1028. HRMS: found 956.4735 $[C_{61}H_{65}NO_9 + H]^+$, calculated for $[C_{61}H_{65}NO_9 + H]^+$ 956.4732. **Step 4:** 2-*O*-(2,3,4,6-Tetra-*O*-benzyl-α-galacto-pyranosyl)-3,4,6-tri-*O*-benzyl-1-deoxynojirimycin (0.2 g, 0.21 mmol) was dissolved in ethanol (6 mL), pH of the solution was adjusted to 2 with 1 M HCl. Pd/C (10 %) was added, the mixture was shacked under H_2 atmosphere at 4 bar for 24 h. The catalyst was filtered through a pad of celite and the solution was concentrated. The residue was purified on gel-filtration column chromatography (eluent: NH_4Ac, 0.15 M, aq.) to obtain pure **29** (35 mg, 0.11 mmol, yield 52 %). ^{1}H NMR (400 MHz, D_2O): δ/ppm = 4.93 (d, J = 3.8 Hz, 1 H, H-1′), 4.05 (t, J = 6.4 Hz, 1 H, H-5′), 3.85 (d, J = 3.2 Hz, 1 H, H-4′), 3.80 (dd, J = 12.8, 3.1 Hz, 1 H, H-6a), 3.77–3.70 (m, 3 H, H-6b, H-2, H-3′), 3.68 (dd, J = 10.5, 3.7 Hz, 1 H, H-2′), 3.58 (d, J = 6.2 Hz, 2 H, H-6′), 3.54 (dd, J = 12.6, 5.0 Hz, 1 H, H-1a), 3.52–3.49 (m, 2 H, H-3, H-4), 3.06 (ddt, J = 8.0, 5.4, 3.1 Hz, 1 H, H-5), 2.84 (dd, J = 12.5, 11.5 Hz, 1 H, H-1b). ^{13}C NMR (100 MHz, D_2O): δ/ppm = 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). $[\alpha]_D^{20}$ = +66.0 (c = 0.10, MeOH). IR: $\tilde{\nu}$/cm^{-1} = 3320, 2954, 2842, 1634, 1393, 1148, 1080, 1014. HRMS: found 364.1010 $[C_{12}H_{23}NO_9 + K]^+$, calculated for $[C_{12}H_{23}NO_9 + K]^+$ 364.1004.

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[1] a) S. Inouye, T. Tsuruoka, T. Niida, *J. Antibiot.* **1966**, *19*, 288–292; b) M. Yagi, T. Kouno, Y. Aoyagi, H. Murai, *J. Agric. Chem. Soc. Jpn.* **1976**, *50*, 571–572; c) S. V. Evans, L. E. Fellows, T. K. M. Shing, G. W. J. Fleet, *Phytochemistry* **1985**, *24*, 1953–1955; d) A. A. Watson, G. W. Fleet, N. Asano, R. J. Molyneux, R. J. Nash, *Phytochemistry* **2001**, *56*, 265–95; e) T. Kajimoto, M. Node, *Curr. Top. Med. Chem.* **2009**, *9*, 13–33; f) T. Thaipitakwong, S. Numhom, P. Aramwit, *Pharm. Biol.* **2018**, *56*, 109–118.

[2] a) N. Asano, K. Oseki, E. Tomioka, H. Kizu, K. Matsui, *Carbohydr. Res.* **1994**, *259*, 243–255; b) N. Asano, T. Yamauchi, K. Kagamifuchi, N. Shimizu, S. Takahashi, H. Takatsuka, K. Ikeda, H. Kizu, W. Chuakul, A. Kettawan, T. Okamoto, *J. Nat. Prod.* **2005**, *68*, 1238–1242; c) N. Asano, T. Yamashita, K. Yasuda, K. Ikeda, H. Kizu, Y. Kameda, A. Kato, R. J. Nash, H. S. Lee, K. S. Ryu, *J. Agric. Food Chem.* **2001**, *49*, 4208–4213; d) A. Kato, N. Kato, S. Miyauchi, Y. Minoshima, I. Adachi, K. Ikeda, N. Asano, A. A. Watson, R. J. Nash, *Phytochemistry* **2008**, *69*, 1261–1265; e) N. Asano, E. Tomioka, H. Kizu, K. Matsui, *Carbohydr. Res.* **1994**, *253*, 235–245.

[3] a) Y. Ezure, *Agric. Biol. Chem.* **1985**, *49*, 2159–2165; b) N. S. Paek, D. J. Kang, H. S. Lee, J. J. Lee, Y. J. Choi, T. H. Kim, K. W. Kim, *Biosci. Biotechnol. Biochem.* **1998**, *62*, 588–589; c) C. Gautheronlenarvor, C.-H. Wong, *J. Chem. Soc., Chem. Commun.* **1991**, 1130–1131; d) M. Kojima, T. Seto, Y. Kyotani, H. Ogawa, S. Kitazawa, K. Mori, S. Maruo, T. Ohgi, Y. Ezure, *Biosci. Biotechnol. Biochem.* **1996**, *60*, 694–696; e) N. Asano, K. Oseki, E. Kaneko, K. Matsui, *Carbohydr. Res.* **1994**, *258*, 255–266.

[4] a) C. Boucheron, S. Toumieux, P. Compain, O. R. Martin, K. Ikeda, N. Asano, *Carbohydr. Res.* **2007**, *342*, 1960–1965; b) H. Furui, M. Kiso, A. Hasegawa, *Carbohydr. Res.* **1992**, *229*, C1–C4; c) M. Kiso, H. Katagiri, H. Furui, A. Hasegawa, *Carbohydr. Res.* **1992**, *11*, 627–644; d) A. Marra, R. Zelli, *Chapter 1 in Carbohydrate Chemistry: Chemical and Biological Approaches*, (Eds.: A. Pilar Rautar, T. Lindhorst, Y. Queneau), Royal Society of Chemistry **2018**, ISBN 978–1–78801–003–0.

[5] a) A. J. Steiner, A. E. Stütz, *Carbohydr. Res.* **2004**, *339*, 2615–2619; b) F. D′ Andrea, G. Catelani, M. Mariani, B. Vecchi, *Tetrahedron Lett.* **2001**, *42*, 1139–1142; c) G. Catelani, F. D′Andrea, L. Puccioni, *Carbohydr. Res.* **2000**, *324*, 204–209.

[6] a) T. Wennekes, R. J. B. H. N. van den Berg, W. Donker, G. A. van der Marel, A. Strijland, J. M. F. G. Aerts, H. S. Overkleeft, *J. Org. Chem.* **2007**, *72*, 1088–1097; b) T. Wennekes, A. J. Meijer, A. K. Groen, R. G. Boot, J. E. Groener, M. van Eijk, R. Ottenhoff, N. Bijl, K. Ghauhalari, H. Song, T. J. Shea, H. Liu, N. Yew, D. Copeland, R. J. B. H. N. van den Berg, G. A. van der Marel, H. S. Overkleeft, J. M. F. G. Aerts, *J. Med. Chem.* **2010**, *53*, 689–698; c) T. Wennekes, B. Lang, M. Leeman, G. A. van der Marel, E. Smits, M. Weber, J. van Wiltenburg, M. Wolberg, J. M. F. G. Aerts, H. S. Overkleeft, *Org. Process Res. Dev.* **2008**, *12*, 414–423.

[7] a) E. W. Baxter, A. B. Reitz, *J. Org. Chem.* **1994**, *59*, 3175–3185; b) A. B. Reitz, E. W. Baxter, *Tetrahedron Lett.* **1990**, *31*, 6777–6780; c) C. R. R. Matos, R. S. C. Lopes, C. C. Lopes, *Synthesis* **1999**, 571–573.

[8] J. Dinkelaar, M. D. Witte, L. J. van den Bos, H. S. Overkleeft, G. A. van der Marel, *Carbohydr. Res.* **2006**, *341*, 1723–1729.

[9] K. Nakagawa, K. Ogawa, O. Higuchi, T. Limura, T. Miyazawa, M. Hori, *Anal. Biochem.* **2010**, *404*, 217–222.

[10] a) J. Dinkelaar, L. J. van den Bos, W. F. J. Hogendorf, G. Lodder, H. S. Overkleeft, J. D. C. Codée, G. A. van der Marel, *Chem. Eur. J.* **2008**, *14*, 9400–9411; b) H. Gold, R. G. Boot, J. M. F. G. Aerts, H. S. Overkleeft, J. D. C. Codée, G. A. van der Marel, *Eur. J. Org. Chem.* **2011**, 1652–1663.

[11] a) S. David, S. Hanessian, *Tetrahedron* **1985**, *41*, 643–663; b) H. Xu, Y. Zhang, H. Dong, Y. Lu, Y. Pei, Z. Pei, *Tetrahedron Lett.* **2017**, *58*, 4039–4042.

[12] a) A. Imamura, H. Ando, S. Korogi, G. Tanabe, O. Muraoka, H. Ishida, M. Kiso, *Tetrahedron Lett.* **2003**, *44*, 6725–6728; b) A. Imamura, H. Ando, H. Ishida, M. Kiso, *Org. Lett.* **2005**, *7*, 4415–4418; c) A. Imamura, A. Kimura, H. Ando, H. Ishida, M. Kiso, *Chem. Eur. J.* **2006**, *12*, 8862–8870.

[13] H. M. Christensen, S. Oscarson, H. H. Jensen, *Carbohydr. Res.* **2015**, *408*, 51–95.

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