The handle http://hdl.handle.net/1887/57984 holds various files of this Leiden University dissertation.

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

GBA2 (EC3.2.1.45, GH116) is a membrane-bound, non-lysosomal retaining β-glucosidase. GBA2 was first described by Matern et al. who annotated the enzyme as a bile acid active glycosidase,¹ but is now widely known to partake in the degradation of glucosylceramide (GlcCer).² GBA2 is associated with a number of physiological and pathological processes, such as neuronal development, lysosomal storage diseases (LSD), tumorigenicity and inflammatory diseases.³
GlcCer is synthesized on the outer endoplasmic reticulum leaflet by glucosylceramide synthase (GCS) from UDP-glucose and ceramide (Figure 1), and degraded in lysosomes by lysosomal glucocerebrosidase (GBA1). In Gaucher disease and Niemann-Pick type C disease (caused by genetic deficiency of GBA1 and acid sphingomyelinase, respectively), GlcCer accumulates in lysosomes, from where it spills over into the cytoplasm where it is degraded by GBA2. This degradation leads to an increase of ceramide concentration in the cytoplasm, which may be responsible for several symptoms observed in patients suffering from Gaucher and Niemann-Pick type C.

Mistry et al. reported that genetic deletion of the GBA2 gene can relieve clinical symptoms in Gaucher diseased mice, which indicates that GBA2 is a potential target for Gaucher disease treatment. This finding is consistent with the hypothesis that compensatory GBA2 overexpression in Gaucher disease has deleterious effects.

Although GBA2 has been identified to be present in various tissues, its expression and activity appears most abundant in the central nervous system. This indicates that GBA2 may play a role in neuronal development. Relevant evidence to support this observation was shown by Martin et al. who demonstrated that the loss of GBA2 function is responsible for motor neuron defects in hereditary spastic paraplegia. Also, mutations in the gene encoding for GBA2 were found in patients suffering from cerebella ataxia, spastic paraplegia, thin corpus callosum and cognitive impairment. These findings underscore the potential correlation between GBA2 and neurodegenerative diseases. GBA2 activity has been connected with tumor biology as well. Inducibly overexpressed GBA2 leads to a decreased anchorage-independent human melanoma cell growth, and thus to the decrease of in vivo melanoma tumor growth. In addition, GBA2 activity has also been associated with inflammatory responses. Mistry et al. reported that GBA2-deficient mice produce significantly lower amounts of several pro-
inflammatory cytokines, which indicates that GBA2 may be a relevant target for drugs aiming for reducing inflammation. For all these reasons, the identification of inhibitors selective for GBA2 is a relevant research objective.

*Figure 2: Structure and IC₅₀ values of the lead compounds.*

*N*-alkyl-deoxynojirimycin derivatives are potent GBA2 inhibitors that however display inhibitory activity against the other GlcCer-metabolizing enzymes, GCS and GBA1, as well (Figure 2). *N*-Butyl-deoxynojirimycin (*N*-butyl-DNJ, Zavesca, 1), a moderately potent GCS inhibitor that at lower concentrations also blocks GBA2 activity, is in clinical use for the treatment of non-neuronopathic Gaucher patients. Inspired by the clinical success of *N*-butyl-DNJ (1), a large number of *N*-alkyl-DNJ derivatives have appeared in the literature and that vary in the nature of the *N*-alkyl group, in the configuration of the polyhydroxylated piperidine or a combination thereof. Amongst these compounds, *N*-adamantanemethyloxypentyl-DNJ (2, MZ-21) and its *l*-ido-configured isoster (3, MZ-31) were identified as very potent GCS inhibitors (much more than the clinical compound, Zavesca 1) that also strongly inhibit GBA2 and to a lesser extend GBA1. In the context of the studies that led to the identification of MZ-21 2 and MZ-31 3, it was observed that *N*-neopentyloxypentyl-DNJ 4 and *N*-neopentyloxypentyl-*l*-ido-DNJ 5, compounds with comparatively (in relation to 2 and 3) smaller *N*-alkyl substituents, are potent GBA2 inhibitors with comparatively less activity against GCS and GBA1. Compared with MZ-21 (IC₅₀ GCS / IC₅₀ GBA2 = 235), compound 4 has a much better GBA2 selectivity (IC₅₀ GCS / IC₅₀ GBA2 = 1020). Compounds 4 and 5 are nanomolar GBA2 inhibitors while inhibiting GCS and GBA1 only in the micromole range, if at all.
**Figure 3:** Structure of the lead N-neopenyloxypentyl-DNJ derivatives 4 (d-glucose configuration) and 5 (l-idose configuration)

Taking compounds 4 and 5 as lead structures and with the aim to investigate whether GBA2 selective inhibitors could be designed, a series d-gluco and l-ido-DNJ derivatives bearing a variety of aliphatic and aromatic N-alkyl substituents (Figure 4) were prepared and evaluated on their potency and selectivity (as compared to GCS and GBA1) as GBA2 inhibitors.

**Figure 4:** d-Gluco and l-ido-DNJ derivatives subject of the here presented studies

Results and discussion

The synthesis of DNJ (9) was accomplished following the established procedure with as key step a double reductive amination of a glucose-derived 5-keto-aldehyde (scheme 1). In the first step, the commercially available 2,3,4,6-tetra-O-benzyl-D-glucopyranose (6) was reduced to give partially protected glucitol 7. Swern oxidation of both the primary and secondary alcohol in 7 followed by double reductive amination gave 2,3,4,6-tetra-O-benzyl-DNJ (8). Catalytic hydrogenation gave DNJ (9) in good yield and sufficient quantities for further elaboration.

Treatment of glucitol 7 with excess methanesulfonyl chloride followed by treatment with allyl amine gave, with inversion of configuration at the carbon bearing the secondary alcohol, fully protected l-ido-DNJ 10 in good overall yield. The allyl protecting group in 10 was removed by potassium tert-butoxide induced isomerization and subsequent acid-catalysed hydrolysis of
the obtained enamine to give 11 in excellent yield. Compound 11 was globally deprotected (H₂, Pd/C) to give L-ido-DNJ 12 for ensuing N-alkylation.

Scheme 1: Synthesis of 1-deoxynojirimycin and L-ido-1-deoxynojirimycin

Reagents and conditions: [a] LiAlH₄, THF; [b] 1) (COCl)₂, DMSO, DCM; 2) HCOONH₄, Na₂SO₄, NaBH₃CN, MeOH, 12% 2 steps; [c] MsCl, pyridine, allyl amine, reflux, 78% 2 steps; [d] tBuOK, DMSO, HCl, 92%; [e] Pd/C, H₂, 82% (9), 76% (12).

The synthesis of appropriately functionalized alkylating agents for preparation of the target compounds was accomplished following established procedures. As an example, the synthesis of tetrahydrofuran-3-ylmethyloxypentyl bromide and its use in the N-alkylation of DNJ 9 and L-ido-DNJ 12 is depicted in Scheme 2. Thus, 1,5-pentanediol (13) was treated with one equivalent of trityl chloride (TrtCl) and base, after which the remaining primary alcohol in 14 was transformed into the sulfonate after reacting with p-toluenesulfonyl chloride (p-TsCl). The tosylate in the thus produced compound 15 was substituted by tetrahydrofuran-3-ylmethyl alcohol, yielding ether 22. The trityl group in 22 was removed and the resulting alcohol 33 subjected to Appel bromination (treatment with triphenylphosphine and tetrabromomethane) to give bromide 44. In a similar fashion, all compounds listed in Figure 5 were prepared. Finally, treatment of DNJ 9 with 44 and diisopropyl ethylamine in DMF gave N-alkyl-DNJ derivative 55, and in a similar vein L-ido-DNJ derivative 62 was prepared (see experimental for details on the alkyl bromide syntheses and ensuing N-alkylation of DNJ 9 and L-ido-DNJ 12).

In a similar way, and in yields varying from 10% up to 88%, N-alkyl-DNJ derivatives 4, 49 - 59 and N-alkyl-L-ido-DNJ 5, 60 - 65 were synthesized (Figure 6).
**Scheme 2**: N-Alkylation strategy of DNJ 9 and L-ido-DNJ 12

![Scheme 2 Diagram]

**Reagents and conditions**: [a] TrtCl, TEA, EtOAc, 85 °C, 3h, 99%; [b] p-TsCl, TEA, DMAP, DCM, 0 °C to r.t., 2h, 70%; [c] 1) THF-3-ylmethanol, NaH, DMF, r.t., 90 min; 2) 15, 75 °C, 1h, 56%; [d] BF₃·OEt₂, toluene/MeOH (1:1), 1.5h, 72%; [e] 1) PPh₃, DCM, r.t., 0 °C; 2) CBr₄, Ar, 2h, 91%; [f] DMF, K₂CO₃, 80 °C, 88% (55), 30% (62).

**Figure 5**: Yields of the syntheses of the alkylation agents and their precursors
**Table 1** shows the inhibitory results of lead structure 4 together with N-alkyl-DNJ derivatives (49 - 59) on the three enzymes involved in glycosylceramide metabolism: GCS, GBA1 and GBA2. From the results on the series of branched alkyl analogues (49 - 51), it can be observed that extending the neopentyl group in 4 with one carbon, as in 51, results in more potent GCS inhibitory activity. The absence (49) or presence (50) of an additional methyl
moeity gave no significant difference in inhibitory potency towards GCS, compared to 4. Within the cycloalkyl series (52 - 54), the compound with the largest substituent proved to be the most potent GCS inhibitor (inhibitory activity: 54 > 53 > 52), whereas the tetrahydrofuran- and tetrahydropyran-modified DNJ derivatives 55 - 57 proved to be poor GCS inhibitors. The thiophene containing iminosugars (58 and 59) inhibit GCS almost as potently as the literature compound, MZ-21 (4). Amongst all the compounds, cyclopentyl-DNJ derivative 54 appeared the most potent GCS inhibitor (IC₅₀ = 0.12), whereas compounds 51, 53, 58 and 59 are also potent GCS inhibitors with sub-micromolar IC₅₀ values. Altogether, these results indicate that a sizeable hydrophobic nonpolar N-alkyl group is critical for GCS activity.

Table 1: GCS, GBA1 and GBA2 IC₅₀ values of the alkylated D-gluco iminosugars

<table>
<thead>
<tr>
<th>Compound</th>
<th>IC₅₀ GCS (µM)</th>
<th>IC₅₀ GBA1 (µM)</th>
<th>IC₅₀ GBA2 (nM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>D-gluco-DNJ series</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>5 ± 0.9</td>
<td>6 ± 0.4</td>
<td>5 ± 0.07</td>
</tr>
<tr>
<td>49</td>
<td>4 ± 0.1</td>
<td>17 ± 1</td>
<td>7 ± 1</td>
</tr>
<tr>
<td>50</td>
<td>6 ± 0.9</td>
<td>3 ± 0.2</td>
<td>4 ± 0.2</td>
</tr>
<tr>
<td>51</td>
<td>0.8 ± 0.03</td>
<td>4 ± 0.009</td>
<td>5 ± 0.3</td>
</tr>
<tr>
<td>52</td>
<td>7 ± 1</td>
<td>51 ± 2</td>
<td>18 ± 0.2</td>
</tr>
<tr>
<td>53</td>
<td>0.6 ± 0.03</td>
<td>12 ± 0.2</td>
<td>9 ± 0.9</td>
</tr>
<tr>
<td>54</td>
<td>0.1 ± 0.06</td>
<td>6 ± 0.4</td>
<td>4 ± 0.2</td>
</tr>
<tr>
<td>55</td>
<td>&gt;50</td>
<td>156 ± 6</td>
<td>42 ± 5</td>
</tr>
<tr>
<td>56</td>
<td>&gt;50</td>
<td>325 ± 14</td>
<td>120 ± 8</td>
</tr>
<tr>
<td>57</td>
<td>10 ± 0.7</td>
<td>63 ± 2</td>
<td>35 ± 2</td>
</tr>
<tr>
<td>58</td>
<td>0.4 ± 0.06</td>
<td>11 ± 0.2</td>
<td>4 ± 0.6</td>
</tr>
<tr>
<td>59</td>
<td>0.4 ± 0.05</td>
<td>6 ± 0.2</td>
<td>2 ± 0.1</td>
</tr>
</tbody>
</table>

With respect to GBA1 inhibitory activity, it was observed that with the exception of compounds 50, 51, 54 and 59, most compounds are less potent than lead compound 4. This may suggest that a nonpolar hydrophobic moiety of a certain size is essential for GBA1 inhibitory activity. Looking at the nature of the alkyloxy substituent, branched alkyl moieties are favorable with respect to GBA1 inhibitory activity (inhibitory potency: 50 > 4 > 49). From the cycloalkyl series, it can be concluded that the larger the substituent is, the more potent the compound inhibits GBA1 (inhibitory potency: 54 > 53 > 52). As was observed for GCS inhibition, the tetrahydrofuranyl/tetrahydropyran-DNJ derivatives are poor GBA1 inhibitors (compare, for instance, the GBA1 inhibition values measured for cyclopentany1-DNJ derivative
54 with those obtained for tetrahydrofuranyl-DNJ derivatives 55 and 56. Another observed trend is that an extra methylene moiety (4 versus 51, 58 versus 59) is beneficial for GBA1 inhibitory activity. The most potent GBA1 inhibitor of this series finally appeared to be compound 50.

Table 2: GCS, GBA1 and GBA2 IC\(_{50}\) values of the alkylated L-ido iminosugars

<table>
<thead>
<tr>
<th>Compound</th>
<th>IC(_{50}) GCS (µM)</th>
<th>IC(_{50}) GBA1 (µM)</th>
<th>IC(_{50}) GBA2 (nM)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>L-ido-DNJ series</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>3 ± 0.1</td>
<td>&gt;1000</td>
<td>10 ± 0.3</td>
</tr>
<tr>
<td>60</td>
<td>5 ± 0.1</td>
<td>196 ± 15</td>
<td>7 ± 0.5</td>
</tr>
<tr>
<td>61</td>
<td>0.12 ± 0.005</td>
<td>176 ± 16</td>
<td>3 ± 0.1</td>
</tr>
<tr>
<td>62</td>
<td>1 ± 0.2</td>
<td>&gt;1000</td>
<td>25 ± 0.7</td>
</tr>
<tr>
<td>63</td>
<td>2.5 ± 0.4</td>
<td>&gt;1000</td>
<td>21 ± 4</td>
</tr>
<tr>
<td>64</td>
<td>0.05 ± 0.002</td>
<td>328 ± 26</td>
<td>2 ± 0.3</td>
</tr>
<tr>
<td>65</td>
<td>0.12 ± 0.008</td>
<td>205 ± 0.4</td>
<td>11 ± 0.04</td>
</tr>
</tbody>
</table>

Looking at GBA2 inhibitory activity, finally, it can be seen that all N-alkyl-DNJ derivatives tested are potent GBA2 inhibitors. Again, compounds 55, 56, and 57 featuring a tetrahydrofuranyl/tetrahydropyranyl moiety are the weakest inhibitors of the series. However, GBA2 inhibitory activity is less affected by the presence of an oxygen atom than GBA1 and GCS inhibitory activities. When comparing tetrahydrofuranyl-DNJ 55 with cyclopentyl-DNJ 54, it can be seen that substituting one of the cyclopentyl carbons (as in 54) for oxygen (as in 55) led to a 500-fold decrease in GCS inhibitory activity, a 25-fold decrease in GBA1 inhibitory activity, and a 10-fold decrease in GBA2 inhibitory activity. Thus, while compound 55 is less potent than carbon analogue 54, it is the more selective GBA2 inhibitor. Amongst the cycloalkyl-DNJ derivatives, compound 54 featuring a cyclopentane moiety appeared to be the most potent GBA2 inhibitor.

In summary on this part, DNJ derivative 55 appears to be the most GBA2 selective compound (IC\(_{50}\) GCS / IC\(_{50}\) GBA2 = 1176, IC\(_{50}\) GBA1 / IC\(_{50}\) GBA2 = 3682), and while less active it is also more selective than compound 4, which served as the starting point of the here-presented studies (IC\(_{50}\) GCS / IC\(_{50}\) GBA2 = 1020, IC\(_{50}\) GBA1 / IC\(_{50}\) GBA2 = 1252). At the same time, all DNJ derivatives follow the general trend that, in case GCS is inhibited, also GBA1 is inhibited with considerable potency. As has been shown before, altering the configuration of the piperidine moiety from d-glucose to L-idose can abolish GBA1 inhibition.
Accordingly, a number of alkyl substituents were selected and the corresponding \textit{N}-alkyl-\textit{L}-ido-DNJ derivatives were prepared (Scheme 2) and evaluated (Table 2) as GCS/GBA1/GBA2 inhibitors. As \textit{N}-alkyl moieties, the most effective substituents from the \textit{D}-gluco-DNJ series in terms of activity and selectivity were selected, leading to compounds 60 – 65, the inhibitory potency of which was compared with lead \textit{L}-ido-DNJ derivative 5. All \textit{L}-ido derivatives tested are more potent GCS inhibitors in comparison with their \textit{D}-gluco congeners. This follows the trend witnessed in earlier studies, and the same holds true for GBA1 inhibition (all \textit{L}-ido-DNJ derivatives tested are considerably weaker GBA1 inhibitors compared to the \textit{D}-gluco-DNJ analogues). Finally and importantly, there is not much difference between GBA2 inhibitory potency when going from a \textit{D}-gluco-DNJ derivative to its configurational \textit{L}-ido-DNJ derivative (compare the GBA2 inhibitory potency of 60 with that of 50; 61 with 54; 62 with 55; 63 with 56; 64 with 58; and 65 with 59). Hence all \textit{L}-ido-DNJ derivatives tested are potent GCS/GBA2 inhibitors with a considerable therapeutic window towards GBA1 – the enzyme one would like to avoid targeting when aiming for the development of new and improved substrate reduction therapies for Gaucher patients. Amongst the compounds tested thiophene-DNJ derivative 64 appears to be the most potent analogue and further testing of this compound in relevant biological systems may be considered.

\section*{Conclusion}

In this Chapter 17 new \textit{N}-alkyl-DNJ derivatives are described, the structures of which are inspired by neopentyl-DNJ derivatives 4 and 5. From the compounds tested, DNJ derivative 55 may well be the most selective, nanomolar GBA2 inhibitor reported to date. The most potent GBA2 inhibitors in turn appear to be 59 and 64. These compounds, as well as thiophene-\textit{L}-ido-DNJ derivative 58, which came out as the most most potent GCS inhibitor, deserves more in-depth studies with respect to their \textit{in situ} and even \textit{in vivo} efficacy to modulate GlcCer metabolism through inhibition of GCS and/or GBA2.

\section*{Experimental Section}

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

\textbf{GCS:} IC$_{50}$ values for GCS activity were measured using living cells with NBD-ceramide as substrate.$^{17}$ Briefly, cells were incubated with 50 nmol C6-NBD-ceramide (6-[\textit{N}-methyl-\textit{N}-(7-nitrobenz-2-oxa-1,3-diazol-4-yl)aminododecanoyl]sphingosine) in the presence of increasing compound concentrations. The cells were harvested after 2h followed by lipid extraction. The formed C6-NBD-glucosylceramide was quantified using a Molecular Dynamics Typhoon
phosphor imaging device. IC₅₀ values were determined from the titration curves. The experiment was performed twice.

**GBA1**: IC₅₀ values for lysosomal GBA1 were measured using 4-methylumbeliferyl-β-D-glucoside as substrate. Briefly, recombinant GBA1 was incubated with increasing compound concentrations for 30 min at 0 °C. Enzyme activity was determined with 3.7 mM 4-methylumbeliferyl-β-D-glucopyranoside in Mcllvaine buffer (0.1 M citrate and 0.2 M phosphate buffer), pH 5.2, 0.1% Triton X-100 (v/v) and sodium taurocholate (0.2%, w/v). Assays performed in triplicate were incubated at 37 °C for 30 min and quenched by the addition of glycine/NaOH (0.2 mL, pH 10.6). The amount of liberated 4-methylumbeliferyl was determined with a PerkinElmer Life Sciences LS30 fluorimeter, excitation wavelength 366 nm, emission wavelength 445 nm.

**GBA2**: IC₅₀ values for the non-lysosomal glucocerebrosidase (GBA2) were measured with 4-methylumbeliferyl-β-D-glucoside as substrate. GBA2-rich membrane suspensions were prepared from enzyme-overexpressing HEK cells by sonicating, and the suspension was preincubated for 30 min at 37 °C with conduritol-B-epoxide (1 mM, CBE, Sigma) to inhibit the lysosomal glucocerebrosidase (GBA1). The prepared GBA2-rich suspension was then incubated with increasing compound concentrations for another 30 min, and then incubated with 3.7 mM 4-methylumbeliferyl-β-D-glucoside in Mcllvaine buffer (0.1 M citrate and 0.2 M phosphate buffer), pH 5.8. Assays were incubated at 37 °C for 1 hour and quenched by the addition of glycine/NaOH (0.2 mL, pH 10.6). The amount of liberated 4-methylumbeliferyl was determined with a PerkinElmer Life Sciences LS30 fluorimeter, excitation wavelength 366 nm, emission wavelength 445 nm. Assays were performed in triplicate.

**General compound synthesis, purification and analysis methods**: All solvents and reagents were obtained commercially and used as received unless stated otherwise. Reactions were executed at room temperature unless stated otherwise. Moisture sensitive reactions were performed under argon atmosphere. Water was removed from starting compounds by repetitive coevaporation with toluene. Solvents were removed by evaporation under reduced pressure. DCM, DMF, and THF were dried over activated 4Å molecular sieves for at least 12 hours before use. Compounds were visualized during TLC analyses by UV (254 nm), and with the following staining solutions: aqueous solution of KMnO₄ (5 g/L) and K₂CO₃ (25 g/L). Visualization of hemiacetals and glycosides was achieved by spraying with a solution of 20% H₂SO₄ in ethanol followed by charring at ≈ 200 °C. Column chromatography purification was performed on silica gel (40-63 μm). ¹H and ¹³C-APT NMR spectra were recorded on a Bruker AV 400 (400/100 MHz) or Bruker 600 (600/150 MHz) spectrometer in CDCl₃, MeOD or D₂O. Chemical shifts are given in ppm (δ) relative to TMS as internal standard (¹H NMR in CDCl₃) or the signal of the deuterated solvent.¹⁹ Coupling constants (J) are given in Hz. High resolution mass spectra were recorded by direct injection (2 μL of a 2 μM solution in water/acetonitrile/tert-butanol 1:1:1 v/v/v) on a mass spectrometer (Thermo Finnigan LTQ Orbitrap) equipped with an electrospray ion source with resolution R = 60000 at m/z 400 (mass range m/z = 150-2000). IR spectra were recorded on a Shimadzu FTIR-8300 and are reported in cm⁻¹. Optical rotation were measured on an automatic polarimeter of sodium D-line, at λ =589 nm. Size-exclusion purifications were performed on an ÄKTA-explorer, column size d = 26 mm, l = 60 mm, mobile phase NH₄HCO₃ (0.15 M) in H₂O, flow 1.5 mL/min. HPLC Purification were performed on a Prep LCMS, Gemini from Phenomenex B.V. (C-18, 110 Å, 5 μm, 19 x 150 mm column).

**General procedure A: Substitution of the tosyl group.** A dry solution of alcohol (5 mmol) in DMF (15 mL) was charged with NaH (10 mmol) and stirred for 90 min. Then a dry solution of 15 (4.5 mmol) in DMF (15 mL) was added. The reaction mixture was heated to 75 °C for 1 h.
After complete consumption of the starting material (TLC monitored), the mixture was cooled to room temperature, quenched by the addition of water (3 mL) and concentrated. The residue was dissolved in a mixture of TEAA (0.1 M), EtOAc and sat. aq. NaHCO₃ (80 mL, 2:3:3) and extracted with EtOAc (3 x 30 mL). The organic phase was dried (MgSO₄), filtered and concentrated. Purification by silica gel column chromatography (0 - 10% EtOAc in PE) gave the target compound.

**General Procedure B: Deprotection of the trityl-group.** To a solution of alkoxyl-1-trityloxypentane (2.0 mmol) in toluene/Methanol (1:1, 20 mL, 0.1 M) was added BF₃-Et₂O (3.0 mmol, 1.5 eq). This mixture was stirred for 1.5 h at r.t. After complete consumption of the starting material (TLC monitored), the mixture was diluted with EtOAc (30 mL) and washed with sat. aq. NaHCO₃ (50 mL). The water layer was extracted with EtOAc (3 x 30 mL) and the combined organic layers were dried (MgSO₄), filtered, concentrated and the residue purified by silica gel column chromatography (1:9 → 1:4 → 1:0, EtOAc:PE) to give the pure product.

**General Procedure C: Bromination.** To a solution of alkoxyl-1-pentanol (1 mmol) in DCM (100 mL, 0.01 M) was added PPh₃ (0.40 g, 1.5 mmol, 1.5 eq) and cooled to 0 °C. Then CBr₄ (0.5 g, 1.5 mmol, 1.5 eq) was added and the reaction mixture was stirred at 0 °C until TLC analysis monitored the complete consumption of starting compound. After which Celite was added and the volatiles were evaporated. The residue was purified with silica gel column chromatography (0 - 100% toluene in pentane → 2 - 20% EtOAc in toluene) to give the bromide spacer.

**General Procedure D: Alkylation of iminosugars.** To a mixture of the 1-bromo-5-alkoxy-pentane (0.3 mmol, 1.5 eq) and diisopropylethylamine (DiPEA, 0.1 mL, 0.6 mmol, 3 eq) was added a solution of iminosugar (0.03 g, 0.2 mmol) in DMF (1 mL). The mixture was stirred overnight at 70 °C. After cooling to r.t., the mixture was filtered and concentrated. The crude product was purified using HPLC.

**Synthesis of DNJ and L-ido-DNJ**

**2,3,4,6-Tetra-Benzyl-1-deoxyjirimycin (8):**

A solution of (COCl)₂ (0.70 mL, 8.16 mmol) in dry DCM (5 mL) under argon atmosphere, was cooled to -78 °C. DMSO (0.71 mL, 10.0 mmol) dissolved in dry DCM (5 mL) was added dropwise. After 40 minutes, 7 (1.02 g, 1.88 mmol, co-evaporated with toluene 3 x) in dry DCM (3 mL), was added dropwise to the mixture. The reaction was stirred for 2 hours at -78 °C, after which Et₃N (3.40 mL, 24.4 mmol) was added dropwise. The mixture was gradually warmed to -5 °C after which it was poured into a cooled (0 °C) MeOH solution (50 mL) containing NaCNBH₃ (0.50 g, 8.00 mmol), HCOONH₄ (2.53 g, 40.1 mmol), and Na₂SO₄ (0.89 g, 6.24 mmol). The mixture was stirred overnight during which the reaction mixture was allowed to warm up to r.t. TLC analysis showed complete consumption of the starting material (1:1, PE:EtOAc, Rᵢ = 0.36). After filtration, the volatiles were evaporated, and the residue was dissolved in EtOAc (70 mL), washed with sat. aq. NaHCO₃ (70 mL). The organic layer was dried (Na₂SO₄) filtered and concentrated. The residue was purified with silica gel column chromatography (2:1 → 1:2, PE:EtOAc) to give the pure product 8 in 12% overall yield (0.114 g, 0.218 mmol). Rᵢ = 0.36 (1:1, PE:EtOAc). ¹H NMR (400 MHz, CDCl₃) δ 7.41 – 7.13 (m, 20H, Ar-Bn), 5.00 – 4.38 (m, 8H, 4 x CH₂ Bn), 3.66 (dd, J = 9.0, 2.5 Hz, 1H, H-6a), 3.58 – 3.44 (m, 3H, H-2, H-3, H-6b), 3.35 (t, J = 9.2 Hz, 1H, H-4), 3.23 (dd, J = 12.3, 4.9 Hz, 1H, H-1a), 2.71 (ddd, J = 9.7, 5.9, 2.6 Hz, 1H, H-5), 2.49 (dd, J = 12.2, 10.3 Hz, 1H, H-1b). ¹³C NMR (100 MHz, CDCl₃) δ 138.9 – 138.0 (Cᵣ Bn), 128.4 – 127.6 (CHᵣ Bn), 87.3 (C-3), 80.6 (C-2), 80.1 (C-4), 75.7, 75.2, 73.4, 72.8 (4 x CH₂ Bn), 70.2 (C-6), 59.8 (C-5), 48.1 (C-1).
1-Deoxynojirimycin (9):

8 (2.00 g, 3.82 mmol) was dissolved in EtOH (120 mL) and pH was adjusted to 2 with HCl solution (1 M). The solution was flushed with argon (3 x), after which two spatula tips of Pd/C (20%) was added. Then the mixture was exposed to H₂ atmosphere (4 bar) for 24 hours. The catalyst was filtered through a pad of Celite and the filtrate was concentrated. The residue was purified on silica gel column chromatography (4:1, EtOAc:H₂O → 1:1, EtOH:H₂O:MeOH + 1% NH₄OH → 6:4:1) to give 9 in 82% yield (511 mg, 3.13 mmol). ¹H NMR (400 MHz, MeOD) δ 3.92 (dd, J = 10.9, 3.1 Hz, 1H, H-6a), 3.67 (dd, J = 10.9, 6.5 Hz, 1H, H-6b), 3.49 (dd, J = 10.6, 8.7, 5.1 Hz, 1H, H-2), 3.28 (t, J = 8.1 Hz, 1H, H-3), 3.24 (t, J = 9.1 Hz, 1H, H-4), 3.18 (dd, J = 12.1, 5.1 Hz, 1H, H-1a), 2.54 (dd, J = 9.4, 6.4, 3.1 Hz, 1H, H-5), 2.52 (dd, J = 12.1, 10.7 Hz, 1H, H-1b). ¹³C NMR (100 MHz, MeOD) δ 81.5 (C-1), 73.5 (C-2), 64.0 (C-6), 63.7 (C-5), 51.9 (C-1).

2,3,4,6-Tetra-O-benzyl-idol-ido-1-deoxynojirimycin (10):

MsCl (4.2 mL, 53.1 mmol) was added dropwise to a cooled mixture (0 °C) of pyridine (90 mL) and 7 (11.5 g, 21.2 mmol). The mixture was stirred for 3 hours at r.t., after which TLC analysis (2:1, PE:EtOAc, Rₖ = 0.13) showed complete consumption of the starting material. Water (60 mL) was added and the solution was concentrated. The residue was dissolved in EtOAc (130 mL), and successively washed with HCl (100 mL, 1M, 2 x), sat. aq. NaHCO₃ (100 mL) and brine (100 mL). The organic layer was dried (Na₂SO₄), filtered and concentrated. The residue was dissolved with toluene (3 x) and allylamine (90 mL) was added to dissolve the methanesulfonylated product, and the solution was heated to reflux for 14 hours, until TLC analysis (2:1, PE:EtOAc) showed complete consumption of the starting material. After concentration, the residue was dissolved with EtOAc (110 mL), washed with sat. aq. NaHCO₃ (100 mL, 2 x) and brine (100 mL). The organic layer was dried (Na₂SO₄), filtered and concentrated. The residue was purified on silica gel column chromatography (17:3, PE:EtOAc) to give 10 in 78% yield (9.30 g, 16.5 mmol). Rₖ = 0.76 (2:1, PE:EtOAc). ¹H NMR (400 MHz, CDCl₃) δ 7.42 – 7.27 (m, 20H, H₆, Bn), 5.77 (ddt, J = 16.8, 10.3, 6.3 Hz, 1H, H-2”), 5.12 (dd, J = 23.6, 6.2 Hz, 2H, H-3”), 4.90 – 4.46 (m, 8H, 4 x CH₂ Bn), 3.84 (dd, J = 10.2, 6.8 Hz, 1H, H-1a”), 3.72 (dd, J = 10.2, 2.5 Hz, 1H, H-1b”), 3.69 (dd, J = 7.6, 4.2 Hz, 1H, H-4), 3.60 – 3.50 (m, 2H, H-2, H-3), 3.42 (ddd, J = 10.1, 5.8, 1.6 Hz, 1H, H-5), 3.37 (dd, J = 6.9, 2.0 Hz, 1H, H-6a), 3.18 (dd, J = 14.1, 6.9 Hz, 1H, H-6b), 2.92 (dd, J = 11.9, 4.9 Hz, 1H, H-1a), 2.53 (dd, J = 11.8, 9.8 Hz, 1H, H-1b). ¹³C NMR (100 MHz, CDCl₃) δ 139.3, 138.8, 138.7, 138.6 (4 x C₆ Bn), 136.3 (C-2”), 128.5 – 127.6 (CH₆ Bn), 117.2 (C-3”), 83.1 (C-4), 80.2 (C-3), 78.9 (C-2), 75.5, 73.4, 73.1 72.8 (4 x CH₂ Bn), 64.7 (C-1”), 60.1 (C-5), 58.1 (C-6), 49.1 (C-1).

2,3,4,6-Tetra-O-benzyl-idol-1-deoxynojirimycin (11):

A mixture of DMSO (35 mL), tBuOK (1.00 g, 8.91 mmol) and 10 (9.30 g, 16.5 mmol), co-evaporated with toluene 3 x) was heated to 100 °C and stirred under argon atmosphere. After 1 hour stirring, HCl solution (30 mL, 1M) was added and the heating resource was removed. After 30 minutes, the mixture was poured into a mixture of sat. aq. NaHCO₃ (100 mL) and Et₂O (150 mL). The organic layer was separated and the water layer was re-extracted with Et₂O (150 mL, 2 x). The combined organic layers were dried (Na₂SO₄), filtered and concentrated. The residue was purified with silica gel column chromatography (2:1 → 1:2 → 0:1, PE:EtOAc) to give the pure product 11 with a yield of 92% (7.93 g, 15.1 mmol). Rₖ = 0.03 (1:1, PE:EtOAc). ¹H NMR (400 MHz, CDCl₃) δ 7.38 – 7.22 (m, 20H, H₆, Bn), 4.68 – 4.49 (m, 8H, 4 x CH₂ Bn), 3.68 (t, J = 9.2 Hz, 1H, H-6a), 3.62 (t, J = 5.3 Hz, 1H, H-3), 3.55 (dd, J = 9.5, 5.2 Hz, 1H, H-6b), 3.45 (td, J = 6.6, 4.1 Hz, 1H, H-2), 3.38 (ddd, J = 8.7, 5.0, 3.6 Hz, 1H, H-5), 3.01 (dd, J = 12.9, 4.1 Hz, 1H, H-1a), 2.86 (dd, J = 12.8, 6.7 Hz, 1H, H-1b). ¹³C NMR (100 MHz, CDCl₃) δ 138.7 – 138.4 (C₆ Bn), 128.5 – 127.7 (CH₆
Bn), 77.3 (C-3), 77.0 (C-2), 74.2 (CH₂ Bn), 73.5 (CH₂ Bn), 72.7 (CH₂ Bn), 72.2 (CH₂ Bn), 67.3 (C-6), 54.7 (C-5), 44.3 (C-1).

L-Ido-1-deoxynojirimycin (12):

11 (2.30 g, 4.39 mmol) was dissolved in EtOH (150 mL) and pH was adjusted to 2 with HCl solution (1 M). The solution was flushed with argon for 3 times, after which two spatula tips of Pd/C (20%) was added. The suspension was exposed to H₂ atmosphere (4 bar) and shaken for 24 hours. The catalyst was filtered through a pad of Celite and the filtrate was concentrated. The residue was purified with silica gel column chromatography (4:1 EtOAc:MeOH + 1% NH₄OH → 6:4:1, EtOH:HO₂:NH₂OH) to give the 12 in 76% yield (840 mg, 3.32 mmol). ¹H NMR (400 MHz, MeOD) δ 3.95 – 3.93 (m, 2H, H-2, H-3), 3.89 (dd, J = 5.7, 2.0 Hz, 1H, H-4), 3.85 (dd, J = 11.0, 2.1 Hz, 1H, H-6a), 3.81 (dd, J = 11.7, 5.1 Hz, 1H, H-6b), 3.47 (ddd, J = 8.9, 5.0, 1.9 Hz, 1H, H-5), 3.36 (dd, J = 13.2, 2.0 Hz, 1H, H-1a), 3.24 (dd, J = 13.2, 1.7 Hz, 1H, H-1b). ¹³C NMR (100 MHz, MeOD) δ 69.2 (C-5), 68.4 (C-3), 68.0 (C-2), 60.3 (C-6), 58.2 (C-5), 46.9 (C-1).

Synthesis of the bromide-spacers

Figure 7: Proton and carbon NMR numbering of the linker molecules (16-48)

5- Trityloxy-1-pentanol (14):

TrtO- OH Trityl chloride (55.82 g, 200 mmol), 1,5-pentanediol (100 mL, 954 mmol), EtOAc (500 mL) and TEA (56 mL, 396 mmol) were mixed. The mixture was stirred for 3h at 85 °C. After complete conversion of the starting material (1:1, PE:EtOAc) the mixture was washed successively with HCl (4 x 100 mL, 1M) and sat. aq. NaHCO₃ (4 x 100 mL), dried (MgSO₄) and concentrated to give compound 22 (68.67 g, 198.20 mmol, 99% yield). Rf = 0.70 (1:1, PE:EtOAc). ¹H NMR (400 MHz, CDCl₃) δ 7.46 – 7.36 (m, 6H, H₆ Trt), 7.29 – 7.17 (m, 9H, H₅ Trt), 3.57 – 3.55 (m, 2H, H-2, H-3), 3.07 – 3.05 (m, 2H, H-2, H-3), 1.65 – 1.63 (m, 2H, H-4), 1.55 – 1.35 (m, 4H, H-2, H-3). ¹³C NMR (100 MHz, CDCl₃) δ 144.4 (C₅ Trt), 128.6 – 126.8 (CH Trt), 86.3 (C₄ Trt), 63.4 (C-1), 62.7 (C-5), 32.5 (C-4), 29.7 (C-2), 22.4 (C-3).

5-(Toluene-4-sulfonyl)-1-trityloxypentane (15):

p-Toluenesulfonyl chloride (8.83 g, 46.3 mmol) was added to a dry and cooled (0 °C) mixture of 14 (10.72 g, 30.94 mmol), TEA (7 mL, 49.5 mmol) and DMAP (0.19 g, 1.56 mmol) in DCM (93 mL). The mixture was stirred for 2h while warming to r.t. The mixture was washed successively with HCl (100 mL, 1M), sat. aq. NaHCO₃ (100 mL) and sat. aq. NaCl (100 mL). The organic phase was dried (MgSO₄), filtered and concentrated. Purification of the residue with silica gel column chromatography (10 – 16% EtOAc in PE) gave compound 15 (10.9 g, 21.7 mmol, 70%) as a white solid. Rf = 0.78 (25% EtOAc in PE). ¹H NMR (400 MHz, CDCl₃) δ 7.75 (d, 2H, H₂ Trt), 7.42 (d, 6H, H₆ Trt), 7.24 – 7.19 (m, 10H, H₅ Trt/Ts), 7.16 – 7.13 (m, 3H, H₃ Trt), 3.94 (t, 2H, H-5), 3.00 (t, 2H, H-1), 1.94 (s, 3H, CH₃ Ts), 1.54 – 1.49 (m, 4H, H-2, H-4), 1.35 – 1.33 (m, 2H, H-3). ¹³C NMR (100 MHz, CDCl₃) δ 144.5 (C₅ Ts), 144.5 (C₄ Trt), 133.3 (C₃ Ts), 130.0 (CH Ts), 128.9 – 127.1 (CH Trt), 86.5 (C₄ Trt), 70.7 (C-5), 63.2 (C-1), 29.4 (C-2), 28.7 (C-4), 22.4 (C-3), 21.7 (CH₃ Ts).

5-(2-Methyl-1-propoxy)-1-trityloxypentane (16):

Compound 15 (4.60 mmol) was subjected to the general procedure A, using 2-methyl-1-propanol (5.05 mmol) to provide 16 (0.77 g, 192
mmol) in a yield of 42%, as thick oil, after silica gel column chromatography purification. $R_f = 0.65$ (10% EtOAc in PE). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.44 (m, J = 8.6, 2.2, 1.6 Hz, 6H, H$_x$ Trt), 7.32 – 7.14 (m, 9H, H$_y$ Trt), 3.37 (t, J = 6.5 Hz, 2H, H$_z$-5), 3.14 (d, J = 6.8 Hz, 2H, H$_z$-6), 3.06 (t, J = 6.6 Hz, 2H, H$_z$-1), 1.84 (dp, J = 6.7 Hz, 1H, H$_z$-7), 1.71 – 1.60 (m, 2H, H$_z$-2), 1.59 – 1.50 (m, 2H, H$_z$-4), 1.50 – 1.37 (m, 2H, H$_z$-3), 0.89 (d, J = 6.7 Hz, 6H, 2x CH$_3$). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 144.6 (C$_q$ Trt), 128.8 (CH Trt), 127.7 (CH Trt), 126.9 (CH Trt), 86.4 (C$_q$ Trt), 77.9 (C-6), 71.0 (C-5), 63.6 (C-1), 30.0 (C-2), 29.7 (C-4), 28.5 (C-7), 23.1 (C-3), 19.5 (2x CH$_3$). IR/cm$^{-1}$: 3061, 2930, 2901, 2866, 1597, 1489, 1448, 1392, 1364, 1176, 1072.

5-(3,3-Dimethyl-2-butoxy)-1-tryloxyptane (17):

![Diagram of 5-(3,3-Dimethyl-2-butoxy)-1-tryloxyptane (17)]

Compound 15 (4.43 mmol) was subjected to the general procedure A, using 3,3-dimethyl-2-butanol (5.06 mmol) to provide 17 (0.95 g, 22.11 mmol) in a 50% yield, as thick oil, after silica gel column chromatography purification. $R_f = 0.79$ (5% EtOAc in PE). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.48 – 7.36 (m, 6H, H$_x$ Trt), 7.28 – 7.11 (m, 12H, H$_y$ Trt), 3.53 (dt, J = 9.4, 5.8 Hz, 1H, H-5a), 3.21 (dd, J = 9.2, 6.2 Hz, 1H, H-5b), 3.06 (t, J = 6.6 Hz, 2H, H-21), 2.93 (q, J = 6.3 Hz, 1H, H-6), 1.74 – 1.35 (m, 6H, H-2, H$_z$-3, H$_z$-4), 1.01 (d, J = 6.3 Hz, 3H, H$_z$-7), 0.87 (s, 9H, H$_z$-9, H$_z$-10, H$_z$-11). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 144.7 (C$_q$ Trt), 128.8 (CH Trt), 127.9 (CH Trt), 126.9 (CH Trt), 86.4 (C$_q$ Trt), 83.4 (C-6), 69.8 (C-5), 63.7 (C-1), 35.3 (C-8), 30.3 (C-2), 30.1 (C-4), 26.2 (C-7), 23.3 (C-3), 14.1 (C-9, C-10, C-11). IR/cm$^{-1}$: 3059, 3022, 2936, 2866, 1597, 1489, 1448, 1389, 1362, 1219, 1090, 1072.

5-(3,3-Dimethyl-1-butoxy)-1-tryloxyptane (18):

![Diagram of 5-(3,3-Dimethyl-1-butoxy)-1-tryloxyptane (18)]

Compound 15 (4.41 mmol) was subjected to the general procedure A, using 3,3-dimethyl-1-butanol (5.07 mmol) to provide 18 (1.02 g, 2.36 mmol) in a 54% yield, as thick oil, after silica gel column chromatography purification. $R_f = 0.67$ (5% EtOAc in PE). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.44 (dt, J = 8.3, 2.2 Hz, 6H, H$_x$ Trt), 7.25 – 7.16 (m, 6H, H$_y$ Trt), 7.16 – 7.10 (m, 3H, H$_z$ Trt), 3.41 (t, J = 7.4 Hz, 2H, H$_z$-5), 3.34 (t, J = 6.4 Hz, 2H, H$_z$-6), 3.06 (td, J = 6.9, 3.0 Hz, 2H, H$_z$-1), 1.63 (p, J = 6.8 Hz, 2H, H$_z$-2), 1.52 (m, 4H, H$_z$-4, H$_z$-7), 1.48 – 1.38 (m, 2H, H$_z$-3), 0.90 (s, 9H, H$_z$-9, H$_z$-10, H$_z$-11). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 144.5 (C$_q$ Trt), 128.7 (C$_A$ Trt), 127.7 (CH Trt), 126.8 (CH Trt), 86.3 (C$_q$ Trt), 70.8 (C-6), 68.1 (C-5), 63.5 (C-1), 43.0 (C-7), 29.8 (C-2), 29.7 (C-9,10,11), 29.6 (C-4), 29.6 (C-8), 23.1 (C-3). IR/cm$^{-1}$: 3057, 3022, 2936, 2864, 1597, 1489, 1448, 1364, 1219, 1111, 1072.

5-(Cyclopropylmethoxy)-1-tryloxyptane (19):

![Diagram of 5-(Cyclopropylmethoxy)-1-tryloxyptane (19)]

Compound 15 (4.41 mmol) was subjected to the general procedure A, using cyclopropylmethanol (5.02 mmol) to provide 19 (0.10 g, 2.49 mmol) in a 56% yield, as thick oil, after silica gel column chromatography purification. $R_f = 0.63$ (10% EtOAc in PE). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.48 – 7.41 (m, 6H, Trt), 7.28 – 7.19 (m, 6H, H$_A$ Trt), 7.20 – 7.13 (m, 3H, H$_B$ Trt), 3.38 (t, J = 6.6 Hz, 2H, H$_C$-5), 3.20 (d, J = 6.9 Hz, 2H, H$_C$-6), 3.06 (t, J = 6.6 Hz, 2H, H$_C$-1), 1.65 (p, J = 6.8 Hz, 2H, H$_C$-2), 1.51 – 1.59 (m, 2H, H$_C$-4), 1.47 – 1.38 (m, 2H, H$_C$-3), 1.08 – 0.97 (m, 1H, H$_C$-7), 0.52 – 0.45 (m, 2H, H$_C$-8), 0.16 (dt, J = 6.0, 4.5 Hz, 2H, H$_C$-9). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 144.6 (C$_q$ Trt), 128.8 (CH Trt), 127.8 (CH Trt), 126.9 (CH Trt), 86.4 (C$_q$ Trt), 75.7 (C-7), 70.7 (C-5), 63.7 (C-1), 30.1 (C-2), 29.8 (C-4), 23.1 (C-3), 10.8 (C-7), 3.2 (C-8, C-9). IR/cm$^{-1}$: 3082, 3057, 3022, 2933, 2862, 1732, 1597, 1489, 1448, 1382, 1219, 1087, 1074.

5-(Cyclobutylmethoxy)-1-tryloxyptane (20):

![Diagram of 5-(Cyclobutylmethoxy)-1-tryloxyptane (20)]

Compound 15 (4.40 mmol) was subjected to the general procedure A, using cyclobutylmethanol (5.01 mmol) to provide 20 (0.79 g, 1.91 mmol) in a 43% yield, as thick oil, after silica gel column chromatography purification. $R_f = 0.74$ (10% EtOAc in PE). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.45 – 7.43 (m, 6H, H$_A$ Trt) 7.22 – 7.17 (m, 6H,
H$_{Ar}$ (Trit), 7.14 – 7.10 (m, 3H, H$_{Ar}$, Trit), 3.37 – 3.32 (m, 4H, H$_2$-5, H$_2$-6), 3.07 (t, 2H, H$_2$-1), 2.56 – 2.49 (m, 1H, C-7), 2.04 – 1.97 (m, 2H, H$_2$-10), 1.86 – 1.79 (m, 2H, H$_2$-8), 1.75 – 1.40 (m, 8H, H$_2$-9, H$_2$-2, H$_2$-4, H$_2$-3). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 144.6 (C$_q$ Trt), 128.9 (CH Trt), 127.9 (CH Trt), 127.0 (CH Trt), 86.5 (C$_q$ Trt), 75.6 (C-6), 71.1 (C-5), 63.7 (C-1), 35.4 (C-7), 29.9 (C-2), 29.8 (C-4), 25.4 (C-8, C-10), 23.2 (C-3), 18.9 (C-9). IR/cm$^{-1}$: 3084, 3059, 2934, 2862, 1597, 1489, 1448, 1363, 1219, 1111, 1072.

5-(Cyclopentylmethoxy)-1-trityloxyypentane (21):

Compound 15 (4.43 mmol) was subjected to the general procedure A, using cyclopentylmethanol (5.09 mmol) to provide 21 (1.29 g, 3.02 mmol) in a 68% yield, as thick oil, after silica gel column chromatography purification. $R_f = 0.77$ (10% EtOAc in PE). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.44 (m, 6H, H$_{Ar}$, Trt), 7.18 – 7.06 (m, 9H, H$_{Ar}$ Trt), 3.39 – 3.29 (m, 2H, H$_2$-5), 3.21 (dd, J = 7.0, 1.0 Hz, 2H, H$_2$-6), 3.05 (dt, J = 11.1, 6.5 Hz, 2H, H$_2$-1), 2.10 (q, J = 7.4 Hz, 1H, H$_2$-7), 1.74 – 1.57 (m, 4H, H$_2$-8, H$_2$-11), 1.57 – 1.36 (m, 8H, H$_2$-2, H$_2$-3, H$_2$-4, H$_2$-9), 1.31 – 1.17 (m, 2H, H$_2$-10). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 144.4 – 125.6 (CH Trt), 75.2 (C-6), 70.6 (C-5), 63.3 (C-1), 38.4 (C-7), 29.4 – 28.7 (C-8, C-9, C-10, C-11), 25.3, 25.1 (C-2, C-4), 22.8 (C-3). IR/cm$^{-1}$: 3084, 3057, 3022, 2939, 2864, 1597, 1489, 1448, 1363, 1176, 1072.

5-(R/S-Tetrahydrofuran-3-ylmethoxy)-1-trityloxyypentane (22):

Compound 15 (4.61 mmol) was subjected to the general procedure A, using R/S tetrahydrofuran-3-ylmethanol (4.96 mmol) to provide 22 (1.11 g, 2.58 mmol) in a 56% yield, as an oil, after silica gel column chromatography purification. $R_f = 0.40$ (15% EtOAc in PE). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.48 – 7.40 (m, 6H, H$_{Ar}$, Trt), 7.21 (dd, J = 8.5, 6.8 Hz, 6H, H$_{Ar}$ Trt), 7.16 – 7.10 (m, 3H, H$_{Ar}$ Trt), 3.75 (ddd, J = 12.1, 8.3, 6.2 Hz, 2H, H$_8$-a, H$_9$-a), 3.68 – 3.55 (m, 1H, H$_8$-b), 3.53 (dd, J = 8.7, 5.4 Hz, 1H, H-9b), 3.40 – 3.18 (m, 4H, H$_2$-5, H$_2$-9), 3.07 (t, J = 6.5 Hz, 2H, H$_2$-1), 2.49 – 2.35 (m, 1H, H-7), 1.87 (ddt, J = 13.9, 8.1, 4.0 Hz, 1H, H-10a), 1.62 (p, J = 6.8 Hz, 2H, H$_2$-2), 1.51 (m, 3H, H$_2$-4, H$_{10b}$), 1.46 – 1.37 (m, 2H, H$_2$-3). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 144.6 (C$_q$ Trt), 128.8 (CH Trt), 127.0 (CH Trt), 86.4 (C$_q$ Trt), 73.0 (C-8), 71.1 (C-5), 71.1 (C-9), 67.8 (C-7), 39.4 (C-1), 30.0 (C-10), 29.6 (C-2), 29.2 (C-4), 23.1 (C-3). IR/cm$^{-1}$: 3445, 2934, 2866, 2347, 1716, 1489, 1448, 1339, 1163, 1074.

5-(R/S-Tetrahydrofuran-1-ylmethoxy)-1-trityloxyypentane (23):

Compound 15 (5.03 mmol) was subjected to the general procedure A, using R/S tetrahydrofuran-1-ylmethanol (5.73 mmol) to provide 23 (1.06 g, 2.46 mmol) in a yield of 49%, as an oil, after silica gel column chromatography purification. $R_f = 0.52$ (15% EtOAc in PE). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.48 – 7.37 (m, 6H, H$_{Ar}$ Trt), 7.32 – 7.23 (m, 6H, H$_{Ar}$ Trt), 7.23 – 7.16 (m, 3H, H$_{Ar}$ Trt), 4.02 (tt, J = 7.3, 5.3 Hz, 1H, H-7), 3.85 (ddd, J = 8.2, 6.9, 6.1 Hz, 1H, H-10a), 3.73 (ddd, J = 8.2, 7.2, 6.3 Hz, 1H, H-10b), 3.53 – 3.37 (m, 4H, H$_2$-5, H$_2$-6), 3.05 (t, J = 6.6 Hz, 2H, H$_2$-1), 1.96 – 1.77 (m, 3H, H$_2$-2, H$_9$-a), 1.69 – 1.60 (m, 2H, H$_2$-2), 1.60 – 1.52 (m, 3H, H$_2$-4, H$_2$-9b), 1.47 – 1.37 (m, 2H, H$_2$-3). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 144.5 (C$_q$ Trt), 128.7 (CH Trt), 127.7 (CH Trt), 126.9 (CH Trt), 86.3 (C$_q$ Trt), 77.9 (C-7), 73.6 (C-6), 71.6 (C-5), 68.4 (C-10), 63.6 (C-1), 30.0 (C-9), 29.6 (C-4), 28.2 (C-8), 25.7 (C-2), 22.9 (C-3). IR/cm$^{-1}$: 3084, 3055, 3022, 2934, 2862, 1597, 1489, 1448, 1373, 1219, 1111, 1074.

5-(Tetrahydro-2H-pyran-4-ylmethoxy)-1-trityloxyypentane (24):

Compound 15 (4.68 mmol) was subjected to the general procedure A, using tetrahydro-2H-pyran-4-ylmethanol (4.34 mmol) to provide 24 (0.79 g, 1.78 mmol) in a yield of 38%, as an oil, after silica gel column chromatography purification. $R_f = 0.48$ (15% EtOAc in PE). $^1$H NMR (400 MHz,
5-(Thiophen-3-methoxy)-1-trityloxyxypentane (25):

Compound 15 (4.56 mmol) was subjected to the general procedure A, using 3-thiophenemethanol (4.57 mmol) to provide 25 (0.73 g, 2.13 mmol) in a 56% yield, as thick oil, after silica gel column chromatography purification. Rf = 0.79 (15% EtOAc in PE). 1H NMR (400 MHz, CDCl3) δ 7.48 - 7.38 (m, 6H, HAr Trt), 7.28 - 7.20 (m, 6H, HAr Trt), 7.20 - 7.14 (m, 3H, Hq Trt), 7.12 (dq, J = 3.0, 1.0 Hz, 1H, H thiophen), 7.04 (dd, J = 4.9, 1.3 Hz, 1H, H thio), 7.02 (dd, J = 4.9, 1.3 Hz, 1H, H thio), 4.44 (d, J = 0.8 Hz, 2H, H-6), 3.40 (t, J = 6.5 Hz, 2H, H-5), 3.05 (t, J = 6.6 Hz, 2H, H-2), 1.70 - 1.49 (m, 4H, H-2, H-4), 1.51 - 1.36 (m, 2H, H-3). 13C NMR (100 MHz, CDCl3) δ 144.5 (Cq Trt), 128.7 (CH Trt), 127.7 (CH Trt), 126.9 (CH Trt), 86.4 (Cq Trt), 75.9 (C-6), 71.1 (C-1), 67.7 (C-9, C-10), 63.5 (C-5), 35.5 (C-7), 30.1 (C-8, C-11), 29.9 (C-2), 29.6 (C-4), 23.0 (C-3). IR/cm⁻¹: 3085, 3056, 3029, 2932, 2849, 1558, 1506, 1506, 1489, 1227, 1163, 1097.

5-(Thiophen-3-ethoxy)-1-trityloxyxypentane (26):

Compound 15 (4.56 mmol) was subjected to the general procedure A, using 3-thiophenemethanol (4.57 mmol) to provide 26 (0.97 g, 1.65 mmol) in a 47% yield, as an oil, after silica gel column chromatography purification. Rf = 0.70 (10% EtOAc in PE). 1H NMR (400 MHz, CDCl3) δ 7.48 - 7.40 (m, 6H, HAr Trt), 7.30 - 7.24 (m, 6H, HAr Trt), 7.22 - 7.19 (m, 3H, Hq Trt), 7.18 - 7.16 (m, 1H, H-thio), 6.97 (dq, J = 3.0, 1.0 Hz, 1H, H thio), 6.94 (dd, J = 4.9, 1.3 Hz, 1H, H thio), 3.53 (t, J = 7.0 Hz, 2H, H-2), 3.41 (t, J = 6.5 Hz, 2H, H-5), 3.05 (t, J = 6.6 Hz, 2H, H-2), 2.92 - 2.84 (m, 2H, H-1), 1.64 (p, J = 6.8 Hz, 2H, H-3), 1.55 (dq, J = 8.7, 6.5 Hz, 2H, H-4), 1.47 - 1.36 (m, 2H, H-2). 13C NMR (100 MHz, CDCl3) δ 144.6 (Cq Trt), 128.9 (CH Trt), 127.9 (CH Trt), 127.4 (CH thio), 127.0 (Cq Trt), 126.0 (CH thio), 122.6 (CH thio), 114.7 (Cq Thio), 86.5 (Cq Trt), 70.4 (C-5), 68.3 (C-6), 63.7 (C-1), 30.0 (C-2), 29.8 (C-4), 23.1 (C-3). IR/cm⁻¹: 3501, 3080, 3059, 3024, 2938, 2864, 2316, 1734, 1448, 1364, 1242, 1068, 1034.

5-(2-Methyl-1-propyloxy)-1-pentanol (27):

Compound 16 (3.56 mmol) was subjected to the general procedure B to provide 27 (0.33 g, 2.07 mmol) in a yield of 73%, as a thick oil, after silica gel column chromatography purification. Rf = 0.24 (20% EtOAc in PE). 1H NMR (400 MHz, CDCl3) δ 3.49 (t, J = 6.6 Hz, 2H, H-2), 3.31 (t, J = 6.5 Hz, 2H, H-5), 3.07 (d, J = 6.8 Hz, 2H, H-6), 1.78 - 1.72 (m, 1H, H-7), 1.53 - 1.43 (m, 4H, H-2, H-4), 1.37 - 1.27 (m, 2H, H-3), 0.81 (s, 3H, Hm-1), 0.79 (s, 3H, Hm-1). 13C NMR (100 MHz, CDCl3) δ 77.8 (C-5), 70.8 (C-5), 62.1 (C-1), 32.3 (C-2), 29.3 (C-4), 28.2 (C-7), 22.3 (C-3), 19.3 (C-8, C-9). IR/cm⁻¹: 3335, 2934, 2859, 1470, 1383, 1366, 1115, 1055, 1007.

5-(3,3-Dimethyl-2-butoxy)-1-pentanol (28):

Compound 17 (2.21 mmol) was subjected to the general procedure B to provide 28 (0.2089 g, 1.11 mmol) in a 50% yield, as an oil, after silica gel column chromatography purification. Rf = 0.32 (20% EtOAc in PE). 1H NMR (400 MHz, CDCl3) δ 3.64 (t, J = 6.6 Hz, 2H, H-2), 3.57 (dt, J = 9.2, 6.1 Hz, 1H, H-5a), 3.26 (dt, J = 9.2, 6.6 Hz, 1H, H-5b), 2.95 (q, J = 6.3 Hz, 1H, H-6), 1.64 - 1.51 (m, 4H, H-2, H-4), 1.50 - 1.36 (m, 2H, H-2), 1.03 (d, J = 6.3 Hz, 3H, H-3). 13C
NMR (100 MHz, CDCl₃) δ 83.4 (C-6), 69.8 (C-5), 62.8 (C-1), 35.1 (C-8), 32.5 (C-2), 29.8 (C-4), 26.0 (C-9, C-10, C-11), 22.5 (C-3), 14.0 (C-7). IR/cm⁻¹: 3296, 2938, 2866, 1474, 1456, 1388, 1371, 1339, 1209, 1099, 1057.

5-(3,3-Dimethyl-1-butoxy)-1-pentanol (29):

Compound 18 (2.36 mmol) was subjected to the general procedure B to provide 29 (0.2142 g, 1.14 mmol) in a yield of 48%, as an oil, after silica gel column chromatography purification. Rf = 0.22 (20% EtOAc in PE). ¹H NMR (400 MHz, CDCl₃) δ 3.63 (t, J = 6.5 Hz, 2H, H₂-1), 3.51 – 3.36 (m, 4H, H₂-5, H₂-2), 1.60 (dq, J = 14.6, 6.6 Hz, 4H, H₂-2, H₂-4), 1.54 – 1.49 (m, 2H, H₂-1), 1.48 – 1.37 (m, 2H, H₂-3), 0.92 (s, 9H, H₃-9, H₃-10, H₃-11). ¹³C NMR (100 MHz, CDCl₃) δ 70.9 (C-6), 68.2 (C-5), 62.6 (C-1), 42.9 (C-9), 32.4 (C-2), 29.7 (C-9, C-10, C-11), 29.6 (C-8), 29.5 (C-4), 22.5 (C-3). IR/cm⁻¹: 3345, 2938, 2864, 1472, 1364, 1244, 1194, 1113, 1055.

5-(Cyclopropylmethoxy)-1-pentanol (30):

Compound 19 (2.49 mmol) was subjected to the general procedure B to provide 30 (0.19 g, 1.19 mmol) in a yield of 48%, as an oil, after silica gel column chromatography purification. Rf = 0.27 (30% EtOAc in PE). ¹H NMR (400 MHz, CDCl₃) δ 3.63 (t, J = 6.5 Hz, 2H, H₂-1), 3.45 (t, J = 6.6 Hz, 2H, H₂-2), 3.25 (d, J = 6.9 Hz, 2H, H₂-6), 1.61 (m, 4H, H₂-2, H₂-4), 1.49 – 1.36 (m, 2H, H₂-3), 1.12 – 0.98 (m, 1H, H-7), 0.59 – 0.47 (m, 4H, H₂-8, H₂-9). ¹³C NMR (100 MHz, CDCl₃) δ 75.6 (C-6), 70.6 (C-5), 62.5 (C-1) 32.4 (C-2), 29.4 (C-4), 22.4 (C-3), 10.6 (C-7), 3.0 (C-8, C-9). IR/cm⁻¹: 3348, 2934, 2858, 1456, 1382, 1339, 1107, 1051.

5-(Cyclobutylmethoxy)-1-pentanol (31):

Compound 20 (1.91 mmol) was subjected to the general procedure B to provide 31 (0.18 g, 1.02 mmol) in a yield of 53%, as an oil, after silica gel column chromatography purification. Rf = 0.41 (30% EtOAc in PE). ¹H NMR (400 MHz, CDCl₃) δ 3.61 (t, J = 6.6 Hz, 2H, H₂-1), 3.42 (t, J = 6.5 Hz, 2H, H₂-2), 3.27 (d, J = 7.2 Hz, 2H, H₂-6), 2.17 – 2.13 (m, 1H, H-7), 1.81 – 1.68 (m, 1H, H-8a), 1.64 – 1.50 (m, 7H, H₂-2, H₂-4, H₂-1H, H₂-10, H₂-8b), 1.47 – 1.37 (m, 2H, H₂-3), 1.26 – 1.15 (m, 2H, H₂-9). ¹³C NMR (100 MHz, CDCl₃) δ 75.6 (C-6), 70.9 (C-5), 62.4 (C-1), 39.3 (C-7), 32.4 (C-2), 29.6 (C-8, C-10), 29.3 (C-4), 25.4 (C-9), 22.4 (C-3). IR/cm⁻¹: 3360, 2933, 2858, 1456, 1364, 1113, 1057.

5-(Cyclopentylmethoxy)-1-pentanol (32):

Compound 21 (3.02 mmol) was subjected to the general procedure B to provide 32 (0.27 g, 1.43 mmol) in a yield of 47%, as an oil, after silica gel column chromatography purification. Rf = 0.45 (30% EtOAc in PE). ¹H NMR (400 MHz, CDCl₃) δ 3.63 (t, J = 6.5 Hz, 2H, H₂-1), 3.45 – 3.37 (m, 4H, H₂-5, H₂-6), 2.56 (p, J = 7.5 Hz, 1H, H-7), 2.11 – 2.00 (m, 2H, H₂-8), 1.97 – 1.79 (m, 2H, H₂-11), 1.77 – 1.65 (m, 2H, H₂-9), 1.64 – 1.54 (m, 4H, H₂-2, H₂-4), 1.46 – 1.37 (m, 2H, H₂-3). ¹³C NMR (100 MHz, CDCl₃) δ 75.7 (C-6), 70.9 (C-5), 62.6 (C-1), 35.1 (C-7), 32.4 (C-2), 29.7 (C-8, C-11) 29.3 (C-4), 25.2 (C-9, C-10), 22.4 (C-3). IR/cm⁻¹: 3333, 2939, 2862, 1456, 1373, 1361, 1115, 1057.

5-(R/S-Tetrahydrofuran-3-ylmethoxy)-1-pentanol (33):

Compound 22 (3.56 mmol) was subjected to the general procedure B to provide 33 (0.48 g, 2.56 mmol) in a yield of 72%, as an oil, after silica gel column chromatography purification. Rf = 0.33 (1:2, PE:EtOAc). ¹H NMR (400 MHz, CDCl₃) δ 3.88 – 3.78 (m, 2H, H₂-10a), 3.72 (dt, J = 8.4, 7.2 Hz, 1H, H₂-8b), 3.65 – 3.52 (m, 3H, H₂-1, H-9b), 3.47 – 3.27 (m, 4H, H₂-5, H₂-6), 2.58 – 2.45 (m, 1H, H-7), 2.06 – 1.94 (m, 1H, H-10a), 1.66 – 1.51 (m, 5H, H₂-2, H₂-4, H-10b), 1.47 – 1.35 (m, 2H, H₂-3). ¹³C NMR (100 MHz, CDCl₃) δ 72.8 (C-6), 71.0 (C-5), 70.9 (C-8), 67.6 (C-9), 62.3 (C-1), 39.1 (C-7), 1057.
32.4 (C-2), 29.3 (C-4), 29.0 (C-10), 22.4 (C-3). IR/cm⁻¹: 3385, 2934, 2858, 1456, 1375, 1211, 1113, 1072, 1056.

5-(R/S-Tetrahydrofuran-1-ylmethoxy)-1-pentanol (34):

Compound 23 (2.46 mmol) was subjected to the general procedure B to provide 34 (0.35 g, 1.86 mmol) in a yield of 76%, as an oil, after silica gel column chromatography purification. Rf = 0.28 (1:2, PE:EtOAc). ¹H NMR (400 MHz, CDCl₃) δ 4.04 (ddd, J = 12.4, 6.6, 5.2 Hz, 1H, H-7), 3.87 (dt, J = 8.3, 6.6 Hz, 1H, H-10a), 3.81 – 3.71 (m, 1H, H-10b), 3.61 (t, J = 6.5 Hz, 2H, H-2), 3.48 (td, J = 6.6, 2.2 Hz, 2H, H-5), 3.44 – 3.39 (m, 2H, H-6), 2.02 – 1.79 (m, 3H, H-2, H-9a, H-8a), 1.66 – 1.54 (m, 5H, H-2, H-9b, H-8b), 1.48 – 1.36 (m, 2H, H-2, H-3). ¹³C NMR (100 MHz, CDCl₃) δ 77.8 (C-7), 73.4 (C-6), 71.4 (C-5), 68.2 (C-10), 62.3 (C-1), 32.4 (C-2), 29.3 (C-3), 28.0 (C-9), 25.5 (C-8), 22.3 (C-3). IR/cm⁻¹: 3410, 2934, 2858, 1645, 1454, 1375, 1109, 1072, 1055.

5-(Tetrahydro-2H-pyran-4-ylmethoxy)-1-pentanol (35):

Compound 24 (1.78 mmol) was subjected to the general procedure B to provide 35 (0.14 g, 0.697 mmol) in a yield of 39%, as an oil, after silica gel column chromatography purification. Rf = 0.31 (1:2, PE:EtOAc). ¹H NMR (400 MHz, CDCl₃) δ 3.96 (m, 2H, H-9a, 10a), 3.60 (t, J = 6.6 Hz, 2H, H-1), 3.45 – 3.34 (m, 4H, H-2, H-9b, H-10b), 3.25 (d, J = 6.6 Hz, 2H, H-6), 1.83 (t, J = 3.4 Hz, 1H, H-7), 1.70 – 1.51 (m, 6H, H-2, H-4, H-8a, H-11a), 1.46 – 1.36 (m, 2H, H-2), 1.36 – 1.21 (m, 2H, H-8b, H-11b). ¹³C NMR (100 MHz, CDCl₃) δ 75.9 (C-6), 71.0 (C-5), 67.6 (C-9, C-10), 62.3 (C-1), 35.3 (C-7), 32.4 (C-2), 29.9 (C-8, C-11), 29.3 (C-4), 22.4 (C-3). IR/cm⁻¹: 3445, 2931, 2851, 1437, 1364, 1236, 1117, 1092, 1012.

5-(Thiophen-3-methoxy)-1-pentanol (36):

Compound 25 (2.13 mmol) was subjected to the general procedure B to provide 36 (0.23 g, 1.15 mmol) in a yield of 69%, as an oil, after silica gel column chromatography purification. Rf = 0.27 (30% EtOAc in PE). ¹H NMR (400 MHz, CDCl₃) δ 7.28 (dd, J = 4.9, 3.0 Hz, 1H, H thioc), 7.19 (ddd, J = 2.1, 1.5, 0.9 Hz, 1H, H thio), 7.06 (dd, J = 4.9, 1.3 Hz, 1H, H thio), 4.49 (s, 2H, H-6), 3.57 (t, J = 6.6 Hz, 2H, H-2), 3.46 (t, J = 6.5 Hz, 2H, H-2), 1.66 – 1.57 (m, 2H, H-4), 1.57 – 1.50 (m, 2H, H-2), 1.45 – 1.36 (m, 2H, H-3). ¹³C NMR (100 MHz, CDCl₃) δ 139.6 (C₅ thio), 127.3 (CH thio), 125.9 (CH thio), 122.7 (CH thio), 70.2 (C-5), 68.1 (C-6), 62.4 (C-1), 32.4 (C-2), 29.4 (C-4), 22.4 (C-3).

5-(Thiophen-3-ethoxy)-1-pentanol (37):

Compound 26 (1.65 mmol) was subjected to the general procedure B to provide 37 (0.3318 g, 1.55 mmol) in a 73% yield, as an oil, after silica gel column chromatography purification. Rf = 0.30 (30% EtOAc in PE). ¹H NMR (400 MHz, CDCl₃) δ 7.23 (dd, J = 4.9, 3.0 Hz, 1H, H thio), 7.01 (dq, J = 3.0, 1.0 Hz, 1H, H thio), 6.97 (dd, J = 4.9, 1.3 Hz, 1H, H thio), 3.62 (m, 4H, H-6, H-7), 3.45 (t, J = 6.5 Hz, 2H, H-5), 2.90 (td, J = 7.0, 0.8 Hz, 2H, H-1), 1.65 – 1.52 (m, 4H, H-2, H-4), 1.45 – 1.35 (m, 2H, H-3). ¹³C NMR (100 MHz, CDCl₃) δ 139.28 (C₅ thio), 128.5 (CH thio), 125.2 (CH thio), 121.1 (CH thio), 71.0 (C-7), 70.9 (C-5), 62.6 (C-6), 32.4 (C-4), 30.7 (C-1), 29.4 (C-2), 22.4 (C-3). IR/cm⁻¹: 3360, 2934, 2860, 1456, 1418, 1348, 1250, 1225, 1155, 1094, 1053.

1-Bromo-5-(2-methyl-1-propyloxy)pentane (38):

Alcohol 27 (2.07 mmol) was subjected to the general procedure C to provide 38 (0.24 g, 1.08 mmol) in a yield of 52% after silica gel column chromatography purification. Rf = 0.71 (100% toluene) ¹H NMR (400 MHz, CDCl₃) δ 3.41 (t, J = 6.9 Hz, 2H, H-2), 3.40 (t, J = 6.3 Hz, 2H, H-2), 3.16 (d, J = 6.7 Hz, 2H, H-6), 1.90 – 1.85 (m, 3H, H-2, H-7), 1.65 – 1.56 (m, 2H, H-4), 1.56 – 1.47 (m, 2H, H-2), 0.92 (s, 3H, H₃-8), 0.89(s, 3H, H₃-7).
9). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 77.9 (C-6), 70.6 (C-5), 33.7 (C-1), 32.6 (C-2), 28.9 (C-4), 28.4 (C-7), 25.0 (C-3), 19.4 (C-8, C-9). IR/cm$^{-1}$: 2940, 2863, 1473, 1363, 1332, 1100.

**1-Bromo-5-(3,3-dimethyl-2-butoxy)pentane (39):**

Alcohol 28 (1.11 mmol) was subjected to the general procedure C to provide 39 (0.25 g, 0.99 mmol) in a yield of 89% after silica gel column chromatography purification. $R_f = 0.71$ (1:1, PE:toluene). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.56 (dt, $J = 9.5, 5.8$ Hz, 1H, H-5a), 3.41 (t, $J = 6.9$ Hz, 2H, H-2), 2.94 (q, $J = 6.3$ Hz, 1H, H-6), 1.88 (p, $J = 7.0$ Hz, 2H, H-2), 1.64 – 1.44 (m, 4H, H-2, H-4), 1.03 (d, $J = 6.3$ Hz, 3H, H-3), 0.87 (s, 9H, H-3, H-2, H-1). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 83.3 (C-6), 69.3 (C-5), 35.1 (C-8), 33.8 (C-1), 32.7 (C-2), 29.3 (C-4), 26.0 (C-9, C-10, C-11), 25.1 (C-3), 13.9 (C-7). IR/cm$^{-1}$: 2938, 2866, 1477, 1369, 1335, 1099.

**1-Bromo-5-(3,3-dimethyl-1-butoxy)pentane (40):**

Alcohol 29 (1.14 mmol) was subjected to the general procedure C to provide 40 (0.14 g, 0.54 mmol) in a yield of 48% after silica gel column chromatography purification. $R_f = 0.71$ (100% toluene). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.50 – 3.38 (m, 6H, H-2, H-5, H-6), 1.96 – 1.84 (m, 2H, H-2, 1.67 – 1.56 (m, 2H, H-2), 1.59 – 1.40 (m, 4H, H-2, H-4), 0.93 (s, 9H, H-3, H-2, H-1). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 70.6 (C-6), 68.2 (C-5), 43.0 (C-7), 33.7 (C-1), 32.7 (C-2), 29.8 (C-9, C-10, C-11), 29.6 (C-8), 29.0 (C-4), 25.0 (C-3). IR/cm$^{-1}$: 2951, 2862, 1734, 1486, 1364, 1111.

**1-Bromo-5-(cyclopropylmethoxy)pentane (41):**

Alcohol 30 (1.19 mmol) was subjected to the general procedure C to provide 41 (0.12 g, 0.54 mmol) in a yield of 46% after silica gel column chromatography purification. $R_f = 0.52$ (100% toluene). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.44 (t, $J = 6.4$ Hz, 2H, H-5), 3.42 (t, $J = 6.8$ Hz, 2H, H-2), 3.25 (dd, $J = 6.9$ Hz, 2H, H-6), 1.89 (dt, $J = 14.8, 7.0$ Hz, 2H, H-2), 1.67 – 1.56 (m, 2H, H-2), 1.58 – 1.47 (m, 2H, H-3), 1.13 – 0.98 (m, 1H, H-7), 0.58 – 0.49 (m, 2H, H-8). 0.20 (dt, $J = 6.1, 4.5$ Hz, 2H, H-9). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 75.6 (C-6), 70.3 (C-5), 33.8 (C-1), 32.6 (C-2), 28.9 (C-4), 24.9 (C-3), 10.6 (C-7), 3.0 (C-8, C-9). IR/cm$^{-1}$: 2934, 2857, 1732, 1456, 1381, 1337, 1250, 1107, 1016.

**1-Bromo-5-(cyclobutylmethoxy)pentane (42):**

Alcohol 31 (1.02 mmol) was subjected to the general procedure C to provide 42 (0.1276 g, 0.54 mmol) in a yield of 53% after silica gel column chromatography purification. $R_f = 0.67$ (100% toluene). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.41 (t, $J = 6.7$ Hz, 2H, H-5), 3.41 (t, $J = 6.9$ Hz, 2H, H-2), 3.38 (dd, $J = 6.8$ Hz, 2H, H-6), 2.60 – 2.54 (m, 1H, H-7), 2.14 – 2.01 (m, 2H, H-2), 1.97 – 1.81 (m, 4H, H-2, H-10), 1.80 – 1.67 (m, 2H, H-9), 1.66 – 1.56 (m, 2H, H-4), 1.56 – 1.45 (m, 2H, H-3). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 75.6 (C-6), 70.7 (C-5), 35.2 (C-7), 33.8 (C-1), 32.6 (C-2), 28.9 (C-4), 25.2 (C-8, C-10), 24.9 (C-3), 18.6 (C-9). IR/cm$^{-1}$: 2932, 2855, 1732, 1456, 1364, 1246, 1111.

**1-Bromo-5-(cyclopentylmethoxy)pentane (43):**

Alcohol 32 (1.43 mmol) was subjected to the general procedure C to provide 43 (0.25 g, 1.01 mmol) in a yield of 71% after silica gel column chromatography purification. $R_f = 0.71$ (100% toluene). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.43 (dd, $J = 6.7, 6.0$ Hz, 2H, H-5), 3.43 (t, $J = 6.8$ Hz, 1H, H-1), 3.27 (d, $J = 7.1$ Hz, 2H, H-6), 2.17 – 2.11 (m, 1H, H-7), 1.89 (dt, $J = 14.1, 7.0$ Hz, 2H, H-2), 1.79 – 1.66 (m, 2H, H-2), 1.64 – 1.45 (m, 8H, H-2, H-4, H-11, H-9), 1.29 – 1.16 (m, 2H, H-10). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 75.6 (C-6), 70.6 (C-5), 39.5 (C-7), 33.8 (C-1), 32.6 (C-2), 29.6 (C-8, C-11), 28.9 (C-4), 25.4 (C-9, C-10), 25.0 (C-3). IR/cm$^{-1}$: 2940, 2857, 1734, 1452, 1366, 1250, 1111.
1-Bromo-5-(R/S-tetrahydrofuran-3-ylmethoxy)pentane (44):

Alcohol 33 (1.86 mmol) was subjected to the general procedure C to provide 44 (0.58 g, 2.32 mmol) in a yield of 91% after silica gel column chromatography purification. \( R_f = 0.33 \) (5% EtOAc in PE). \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \( \delta \): 3.87 - 3.78 (m, 2H, H-8a, H-9a), 3.78 - 3.66 (m, 1H, H-8b), 3.56 (dd, \( J = 8.7, 5.4 \) Hz, 1H, H-9b), 3.46 - 3.25 (m, 6H, H-2, H-5, H-6), 2.54 - 2.48 (m, 1H, H-7), 2.06 - 1.94 (m, 1H, H-10a), 1.92 - 1.83 (m, 2H, H-2), 1.65 - 1.54 (m, 3H, H-4, H-10b), 1.54 - 1.45 (m, 2H, H-3). \(^1^C\) NMR (100 MHz, CDCl\(_3\)) \( \delta \): 73.0 (C-6), 71.0 (C-9), 70.8 (C-5), 67.7 (C-8), 39.2 (C-7), 33.7 (C-1), 32.6 (C-2), 29.1 (C-10), 28.8 (C-4), 24.9 (C-3). IR/cm\(^{-1}\): 2934, 2857, 1486, 1111, 1076.

1-Bromo-5-(R/S-tetrahydrofuran-1-ylmethoxy)pentane (45):

Alcohol 34 (1.86 mmol) was subjected to the general procedure C to provide 45 (0.33 g, 1.30 mmol) in a yield of 70% after silica gel column chromatography purification. \( R_f = 0.33 \) (5% EtOAc in PE). \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \( \delta \): 4.04 (m, 1H, H-7), 3.88 (m, 1H, H-10a), 3.75 (m, 1H, H-10b), 3.49 (m, 2H, H-5), 3.47-3.39 (m, 4H, H-1, H-6), 1.99 - 1.83 (m, 5H, H-2, H-8a, H-9), 1.66-1.62 (m, 3H, H-8b, H-4), 1.61-1.53 (m, 2H, H-3). \(^1^C\) NMR (100 MHz, CDCl\(_3\)) \( \delta \): 77.9 (C-7), 73.6 (C-6), 71.2 (C-5), 68.3 (C-10), 33.8 (C-1), 32.6 (C-2), 28.8 (C-4), 28.1 (C-8), 25.6 (C-9), 24.9 (C-3). IR/cm\(^{-1}\): 2938, 2860, 1456, 1437, 1117, 1070.

1-Bromo-5-(tetrahydro-2H-pyran-4-ylmethoxy)pentane (46):

Alcohol 35 (0.31 mmol) was subjected to the general procedure C to provide 46 (0.061 g, 0.23 mmol) in a yield of 33% after silica gel column chromatography purification. \( R_f = 0.35 \) (5% EtOAc in PE). \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \( \delta \): 4.00 - 3.94 (m, 2H, H-9a, H-10a), 3.45 - 3.35 (m, 6H, H-2, H-5, H-9b, H-10b), 3.25 (d, \( J = 6.6 \) Hz, 2H, H-6), 1.93 - 1.77 (m, 3H, H-2, H-7), 1.68 - 1.55 (m, 4H, H-4, H-8a, H-11a), 1.55 - 1.46 (m, 2H, H-3), 1.42 - 1.19 (m, 2H, H-8b, H-11b). \(^1^C\) NMR (100 MHz, CDCl\(_3\)) \( \delta \): 76.0 (C-6), 70.8 (C-5), 67.8 (C-9, C-10), 35.5 (C-7), 33.8 (C-1), 32.6 (C-2), 30.0 (C-8, C-11), 28.9 (C-4), 24.9 (C-3). IR/cm\(^{-1}\): 2924, 2845, 1734, 1384, 1115, 1092.

1-Bromo-5-(thiophen-3-methoxy)pentane (47):

Alcohol 36 (1.15 mmol) was subjected to the general procedure C to provide 47 (0.19 g, 0.74 mmol) in a yield of 45% after silica gel column chromatography purification. \( R_f = 0.67 \) (100% toluene). \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \( \delta \): 7.33 (dd, \( J = 5.0, 3.0 \) Hz, 1H, H thio), 7.10 (dd, \( J = 5.0, 1.2 \) Hz, 1H, H thio), 4.56 - 4.51 (s, 2H, H-6), 3.50 (t, \( J = 6.3 \) Hz, 2H, H-5), 3.44 (t, \( J = 6.8 \) Hz, 2H, H-1), 1.90 (p, \( J = 7.0 \) Hz, 2H, H-2), 1.72 - 1.59 (m, 2H, H-4), 1.62 - 1.48 (m, 2H, H-3). \(^1^C\) NMR (100 MHz, CDCl\(_3\)) \( \delta \): 139.7 (C\(_\text{thio}\)), 127.3 (CH thio), 126.0 (CH thio), 122.6 (CH thio), 70.0 (C-6), 68.2 (C-5), 33.8 (C-1), 32.6 (C-2), 28.9 (C-4), 25.0 (C-3). IR/cm\(^{-1}\): 3000, 2934, 2857, 1732, 1153, 1096.

1-Bromo-5-(thiophen-3-ethoxy)pentane (48):

Alcohol 37 (1.55 mmol) was subjected to the general procedure C to provide 48 (0.28 g, 0.99 mmol) in a yield of 46% after silica gel column chromatography purification. \( R_f = 0.67 \) (100% toluene). \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \( \delta \): 7.25 - 7.21 (m, 1H, H thio), 7.02 - 6.98 (m, 1H, H thio), 6.97 (dd, \( J = 4.9, 1.3 \) Hz, 1H, H thio), 3.62 (t, \( J = 7.0 \) Hz, 2H, H-6), 3.44 (t, \( J = 6.3 \) Hz, 2H, H-5), 3.39 (t, \( J = 6.8 \) Hz, 2H, H-1), 2.90 (td, \( J = 7.0, 0.8 \) Hz, 2H, H-7), 1.92 - 1.79 (m, 2H, H-2), 1.64 - 1.54 (m, 2H, H-4), 1.53 - 1.44 (m, 2H, H-3). \(^1^C\) NMR (100 MHz, CDCl\(_3\)) \( \delta \): 139.4 (C\(_\text{thio}\)), 128.5 (CH thio), 125.2 (CH thio), 121.1 (CH thio), 71.1 (C-6), 70.6 (C-5), 33.9 (C-1), 32.6 (C-2), 30.8 (C-7), 28.9 (C-4), 25.0 (C-3). IR/cm\(^{-1}\): 3102, 2934, 2857, 1734, 1109.
**Synthesis of the alkylated iminosugars**

*Figure 8: Proton and carbon NMR numbering of iminosugars (4, 5, 49 - 65)*

**N-[5-(3,3-Dimethyl-1-propoxy)pentyl]-1-deoxyoijirimycin (4):**

Bromide 68 (0.30 mmol) was subjected to the general procedure D with 1-deoxyoijirimycin (0.20 mmol) to provide 4 (30 mg, 0.094 mmol, yield 77%). $^1$H NMR (400 MHz, MeOD) $\delta$ 4.07 (d, $J = 12.4$ Hz, 1H, H-6a), 3.93 (dd, $J = 12.5$, 2.9 Hz, 1H, H-6b), 3.67 (td, $J = 10.1$, 4.5 Hz, 1H, H-2), 3.58 (t, $J = 9.6$ Hz, 1H, H-4), 3.47 (t, $J = 6.3$ Hz, 2H, H-5'), 3.43 - 3.24 (m, 3H, H-1a, H-3, H-1'a), 3.22 (d, $J = 6.6$ Hz, 2H, H-2'), 3.10 (br s, 1H, H-1'b), 2.92 - 2.74 (m, 2H, H-5, H-1b), 1.89 - 1.81 (m, 1H, H-7'), 1.80 - 1.72 (m, 2H, H-2'), 1.71 - 1.62 (m, 2H, H-4'), 1.54 - 1.41 (m, 2H, H-3'), 0.93 (d, $J = 6.7$ Hz, 6H, H-3', H-9'). $^{13}$C NMR (100 MHz, MeOD) $\delta$ 77.6 (C-6'), 77.2 (C-3), 70.2 (C-5'), 68.1 (C-4), 67.0 (C-2), 66.1 (C-5), 55.5 (C-6), 54.0 (C-1), 52.6 (C-1'), 28.9 (C-4'), 28.2 (C-7'), 23.3 (C-3'), 22.9 (C-2'), 18.3 (C-8', C-9'). [\(\alpha\)]$_{D}^{20}$ = -7.17 ($c = 0.56$, MeOH), IR/cm$^{-1}$: 3333, 2871, 1670, 1432, 1383, 1201, 1131, 1031. HRMS: found 306.22757 [C$_{15}$H$_{31}$NO$_{5}$H]$^+$, calculated for [C$_{15}$H$_{31}$NO$_{5}$H]$^+$ 306.22750.

**N-[5-(2-Methyl-1-propoxy)pentyl]-1-deoxyoijirimycin (49):**

Bromide 38 (0.30 mmol) was subjected to the general procedure D with 1-deoxyoijirimycin (0.20 mmol) to provide 49 (28 mg, 0.092 mmol, yield 46%). $^1$H NMR (400 MHz, MeOD) $\delta$ 4.07 (d, $J = 12.4$ Hz, 1H, H-6a), 3.93 (dd, $J = 12.5$, 2.9 Hz, 1H, H-6b), 3.67 (td, $J = 10.1$, 4.5 Hz, 1H, H-2), 3.58 (t, $J = 9.6$ Hz, 1H, H-4), 3.47 (t, $J = 6.3$ Hz, 2H, H-5'), 3.43 - 3.24 (m, 3H, H-1a, H-3, H-1'a), 3.22 (d, $J = 6.6$ Hz, 2H, H-2'), 3.10 (br s, 1H, H-1'b), 2.92 - 2.74 (m, 2H, H-5, H-1b), 1.89 - 1.81 (m, 1H, H-7'), 1.80 - 1.72 (m, 2H, H-2'), 1.71 - 1.62 (m, 2H, H-4'), 1.54 - 1.41 (m, 2H, H-3'), 0.93 (d, $J = 6.7$ Hz, 6H, H-3', H-9'). $^{13}$C NMR (100 MHz, MeOD) $\delta$ 77.6 (C-6'), 77.2 (C-3), 70.2 (C-5'), 68.1 (C-4), 67.0 (C-2), 66.1 (C-5), 55.5 (C-6), 54.0 (C-1), 52.6 (C-1'), 28.9 (C-4'), 28.2 (C-7'), 23.3 (C-3'), 22.9 (C-2'), 18.3 (C-8', C-9'). [\(\alpha\)]$_{D}^{20}$ = -7.17 ($c = 0.56$, MeOH), IR/cm$^{-1}$: 3333, 2871, 1670, 1432, 1383, 1201, 1131, 1031. HRMS: found 306.22757 [C$_{15}$H$_{31}$NO$_{5}$H]$^+$, calculated for [C$_{15}$H$_{31}$NO$_{5}$H]$^+$ 306.22750.

**N-[5-(3,3-Dimethyl-2-butoxy)pentyl]-1-deoxyoijirimycin (50):**

Bromide 39 (0.32 mmol) was subjected to the general procedure D with 1-deoxyoijirimycin (0.20 mmol) to provide 50 (31 mg, 0.094 mmol, yield 47%). $^1$H NMR (400 MHz, MeOD) $\delta$ 4.14 (d, $J = 12.4$ Hz, 1H, H-6a), 3.93 (dd, $J = 12.6$, 2.7 Hz, 1H, H-6b), 3.72 (td, $J = 10.4$, 4.9 Hz, 1H, H-2),
3.68 – 3.58 (m, 3H, H-3, H-4, H-5’a), 3.48 (dd, J = 12.0, 4.9 Hz, 1H, H-1a), 3.43 – 3.35 (m, 3H, H-1’a, H-3, H-5’b), 3.22 (td, J = 12.2, 5.1 Hz, 1H, H-1’b), 3.07 (br d, J = 9.8 Hz, 1H, H-5), 3.03 (d, J = 6.3 Hz, 1H, H-6’), 3.01 (dd, J = 12.5, 10.9 Hz, 1H, H-1b), 1.81 (dt, J = 11.1, 5.7 Hz, 2H, H-2’), 1.65 (dt, J = 8.8, 5.8 Hz, 2H, H-2’), 1.57 – 1.44 (m, 2H, H-2’, 3’), 1.07 (d, J = 6.3 Hz, 3H, H-3, H-7’), 0.90 (s, 9H, H3-9’, H3-10’, H3-11’). 13C NMR (100 MHz, MeOD) δ 83.3 (C-6’), 76.7 (C-3’), 68.9 (C-5’), 67.4 (C-4), 66.4 (C-2), 66.0 (C-5), 53.5 (C-6), 53.5 (C-1), 52.9 (C-1’), 34.6 (C-4’), 29.3 (C-4’), 25.0 (C-9’, C-10’, C-11’), 23.2 (C-3’), 22.6 (C-2’), 12.8 (C-7’). [α]20° = -6.94 (c = 0.63, MeOH).

IR/cm⁻¹: 3330, 2956, 2875, 1672, 1439, 1203, 1134, 1029. HRMS: found 334.25885 [C17H35NO5+H]+, calculated for [C17H35NO5+H]+ 334.25880.

**N-[5-(3,3-Dimethyl-1-butoxy)pentyl]-1-deoxynojirimycin (51):**

Bromide 40 (0.299 mmol) was subjected to the general procedure D with 1-deoxynojirimycin (0.20 mmol) to provide 51 (28 mg, 0.085 mmol, yield 43%). 1H NMR (400 MHz, MeOD) δ 4.12 (d, J = 12.5 Hz, 1H, H-6a), 3.93 (dd, J = 12.3, 2.8 Hz, 1H, H-6b), 3.71 (td, J = 10.4, 10.0, 4.4 Hz, 1H, H-2), 3.62 (t, J = 9.7 Hz, 1H, H-4), 3.50 (t, J = 7.3 Hz, 2H, H2-6’), 3.50 (dd, J = 9.0, 1.5 Hz, 1H, H-1a), 3.46 (t, J = 6.3 Hz, 2H, H-2’), 3.43 – 3.36 (m, 2H, H-3, H-1’a), 3.22 (td, J = 12.1, 5.2 Hz, 1H, H-1b), 3.07 (br d, J = 10.3 Hz, 1H, H-5), 3.00 (t, J = 11.7 Hz, 1H, H-1b), 1.90 – 1.71 (m, 2H, H2-2’), 1.65 (dd, J = 13.7, 7.5, 6.0 Hz, 2H, H-2’, 4’), 1.51 (t, J = 7.4 Hz, 2H, H-2’), 1.53 – 1.43 (m, 2H, H-3), 0.94 (s, 9H, H3-9’, H3-10’, H3-11’). 13C NMR (100 MHz, MeOD) δ 76.7 (C-3’), 70.0 (C-5’), 67.9 (C-6’), 67.4 (C-4), 66.4 (C-2), 66.0 (C-5), 53.4 (C-6), 53.3 (C-1), 52.9 (C-1’), 42.6 (C-7’), 29.7 (C-4’), 28.7 (C-9’, C-10’, C-11’), 25.8 (C-3), 25.0 (C-2), 22.6 (C-8’). [α]20° = +0.56 (c = 0.57, MeOH).

IR/cm⁻¹: 3343, 2954, 2870, 1673, 1433, 1203, 1134. HRMS: found 334.25886 [C17H35NO5+H]+, calculated for [C17H35NO5+H]+ 334.25880.

**N-[5-(Cyclopropylmethoxy)pentyl]-1-deoxynojirimycin (52):**

Bromide 41 (0.30 mmol) was subjected to the general procedure D with 1-deoxynojirimycin (0.20 mmol) to provide 52 (30 mg, 0.097 mmol, yield 49%). 1H NMR (400 MHz, MeOD) δ 4.13 (d, J = 12.6 Hz, 1H, H-6a), 3.94 (dd, J = 12.7, 3.1 Hz, 1H, H-6b), 3.73 (td, J = 10.3, 4.7 Hz, 1H, H-2), 3.64 (t, J = 9.8 Hz, 1H, H-4), 3.52 (t, J = 6.3 Hz, 2H, H-2’), 3.51 – 3.46 (m, 1H, H-1a), 3.40 (t, J = 9.2 Hz, 1H, H-3), 3.40 – 3.36 (m, 1H, H-1’a), 3.30 (d, J = 6.9 Hz, 2H, H-2), 3.23 (td, J = 12.3, 5.3 Hz, 1H, H-1’b), 3.08 (br d, J = 10.1 Hz, 1H, H-5), 3.01 (t, J = 11.7 Hz, 1H, H-1b), 1.91 – 1.73 (m, 2H, H-2’), 1.72 – 1.63 (m, 2H, H-2’), 1.55 – 1.45 (m, 2H, H-3’), 1.10 – 1.00 (m, 1H, H-7), 0.57 – 0.51 (m, 2H, H-8’), 0.22 (dt, J = 6.1, 4.4 Hz, 2H, H-9’). 13C NMR (100 MHz, MeOD) δ 76.7 (C-3’), 75.3 (C-6’), 69.8 (C-5’), 67.4 (C-4), 66.4 (C-2), 66.0 (C-5), 53.6 (C-6), 53.4 (C-1), 52.9 (C-1’), 28.7 (C-4’), 23.1 (C-3’), 22.5 (C-2’), 10.0 (C-7’), 2.1 (C-8’, C-9’). [α]20° = -6.08 (c = 0.59, MeOH). IR/cm⁻¹: 3346, 2866, 1672, 1430, 1202, 1134, 1032. HRMS: found 304.21194 [C15H29NO5+H]+, calculated for [C15H29NO5+H]+ 304.21185.

**N-[5-(Cyclobutylmethoxy)pentyl]-1-deoxynojirimycin (53):**

Bromide 42 (0.31 mmol) was subjected to the general procedure D with 1-deoxynojirimycin (0.20 mmol) to provide 53 (25 mg, 0.079 mmol, yield 39%). 1H NMR (400 MHz, MeOD) δ 4.14 (d, J = 12.5 Hz, 1H, H-6a), 3.93 (dd, J = 12.7, 3.1 Hz, 1H, H-6b), 3.71 (td, J = 10.7, 10.2, 4.7 Hz, 1H, H-2), 3.63 (t, J = 9.8 Hz, 1H, H-4), 3.49 (t, J = 6.2 Hz, 2H, H-2’), 3.48 (dd, J = 11.8, 5.2 Hz, 1H, H-1a), 3.43 (d, J = 6.8 Hz, 2H, H-2’), 3.43 – 3.36 (m, 1H, H-1’a), 3.39 (t, J = 9.4 Hz, 1H, H-3),
N-[5-(Cyclopentylmethoxy)pentyl]-1-deoxyanojirimycin (54):

Bromide 43 (0.30 mmol) was subjected to the general procedure D with 1-deoxyanojirimycin (0.20 mmol) to provide 54 (23 mg, 0.069 mmol, yield 35%). \(^1\)H NMR (400 MHz, MeOD) \(\delta\) 4.13 (d, \(J = 12.5\) Hz, 1H, H-6a), 3.93 (dd, \(J = 12.6, 3.1\) Hz, 1H, H-6b), 3.72 (dt, \(J = 14.7, 4.6\) Hz, 1H, H-2), 3.63 (t, \(J = 9.7\) Hz, 1H, H-4), 3.52 – 3.44 (m, 1H, H-1a), 3.49 (t, \(J = 6.2\) Hz, 2H, H-2'), 3.43 – 3.35 (m, 2H, H-3, H-1'a), 3.33 (d, \(J = 7.1\) Hz, 2H, H-2'), 3.22 (td, \(J = 12.3, 5.3\) Hz, 1H, H-1b), 2.63 – 2.53 (m, 1H, H-7'), 2.14 – 2.03 (m, 2H, H-8'), 2.03 – 1.91 (m, 2H, H-10''), 1.91 – 1.72 (m, 4H, H-2', H-9'), 1.67 (dddd, \(J = 13.7, 7.5, 5.9\) Hz, 2H, H-2''), 1.51 – 1.47 (m, 2H, H-3'). \(^{13}\)C NMR (100 MHz, MeOD) \(\delta\) 76.7 (C-3), 75.2 (C-6), 70.2 (C-5'), 67.4 (C-4), 66.4 (C-2), 66.0 (C-5), 53.5 (C-6), 53.4 (C-1), 52.9 (C-1'), 35.1 (C-7'), 28.7 (C-4'), 24.6 (C-8', C-9'), 23.1 (C-3'), 22.5 (C-2'), 18.0 (C-10'). \(\alpha^{20}_{D} = -0.62\) (c = 0.50, MeOH). IR/cm\(^{-1}\): 3341, 2938, 2865, 1673, 1431, 1202, 1135, 1031. HRMS: found 318.22761 [C\(_{16}\)H\(_{31}\)NO\(_{5}\)H\(^+\)], calculated for [C\(_{16}\)H\(_{31}\)NO\(_{5}\)H\(^+\)] \(318.22750\).

N-[5-(R/S-Tetrahydrofuran-3-ylmethoxy)pentyl]-1-deoxyanojirimycin (55):

Bromide 44 (0.29 mmol) was subjected to the general procedure D with 1-deoxyanojirimycin (0.20 mmol) to provide 55 (58.5 mg, 0.17 mmol, yield 88%). \(^1\)H NMR (400 MHz, MeOD) \(\delta\) 4.14 (d, \(J = 12.6\) Hz, 1H, H-6a), 3.93 (dd, \(J = 12.4, 3.0\) Hz, 1H, H-6b), 3.85 (dd, \(J = 8.3, 5.5\) Hz, 1H, H-9'a), 3.83 (dd, \(J = 8.7, 7.2\) Hz, 1H, H-10'a), 3.78 – 3.69 (m, 2H, H-9'b, H-2), 3.63 (t, \(J = 9.8\) Hz, 1H, H-4), 3.58 (dd, \(J = 8.6, 5.5\) Hz, 2H, H-10'b), 3.52 – 3.47 (m, 1H, H-1a), 3.50 (td, \(J = 6.3, 1.7\) Hz, 2H, H-5'), 3.44 (dd, \(J = 9.2, 6.3\) Hz, 1H, H-6'a), 3.43 – 3.35 (m, 3H, H-1'a, H-3, H-6'b), 3.20 – 3.18 (m, 1H, H-1'b), 3.07 (br d, \(J = 9.9\) Hz, 1H, H-5), 3.01 (t, \(J = 11.7\) Hz, 1H, H-1b), 2.59 – 2.48 (m, 1H, H-7'), 2.02 – 1.98 (m, 1H, H-8'a), 1.91 – 1.72 (m, 2H, H-2'), 1.72 – 1.60 (m, 3H, H-8'b, H-2''), 1.53 – 1.47 (m, 2H, H-2''), 1.30 – 1.20 (m, 2H, H-1'). \(^{13}\)C NMR (100 MHz, MeOD) \(\delta\) 76.7 (C-3), 72.5 (C-6), 70.5 (C-10'), 70.3 (C-3'), 67.4 (C-4), 67.3 (C-9'), 66.4 (C-2), 66.0 (C-5), 53.3 (C-1), 52.8 (C-8), 29.7 (C-9'), 25.0 (C-4'), 23.1 (C-3'), 22.7 (C-2'). \(\alpha^{20}_{D} = -4.76\) (c = 0.46, MeOH). IR/cm\(^{-1}\): 3346, 2950, 2867, 1673, 1433, 1203, 1133, 1032. HRMS: found 332.24323 [C\(_{17}\)H\(_{33}\)NO\(_{5}\)H\(^+\)], calculated for [C\(_{17}\)H\(_{33}\)NO\(_{5}\)H\(^+\)] \(332.24315\).

N-[5-(R/S-Tetrahydrofuran-1-ylmethoxy)pentyl]-1-deoxyanojirimycin (56):

Bromide 45 (0.29 mmol) was subjected to the general procedure D with 1-deoxyanojirimycin (0.20 mmol) to provide 56 (10 mg, 0.030 mmol, yield 15%). \(^1\)H NMR (600 MHz, MeOD) \(\delta\) 4.12 (d, \(J = 11.5\) Hz, 1H, H-6a), 4.07 – 4.01 (m, 1H, H-7'), 3.91 (dd, \(J = 12.5, 3.2\) Hz, 1H, H-6b), 3.85 (dt, \(J = 8.2, 6.7\) Hz, 1H, H-10'a), 3.76 (td, \(J = 7.7, 6.1\) Hz, 1H, H-10'b), 3.69 – 3.67 (m, 1H, H-2), 3.60 (dd, \(J = 12.7, 6.6\) Hz, 1H, H-4), 3.51 (td, \(J = 6.2, 3.8\) Hz, 1H, H-5'), 3.47 – 3.34 (m, 5H, H-2', H-1'a, H-1'a, H-3), 3.20 (td, \(J = 12.4, 5.0\) Hz, 1H, H-1b), 3.04 (d, \(J = 9.9\) Hz, 1H, H-5), 2.99 (t, \(J = 11.7\) Hz, 1H, H-1'b), 2.01 – 1.95 (m, 1H, H-8'a), 1.94 – 1.87 (m, 1H, H-9'), 1.87 – 1.71 (m, 2H,
**N-[5-(Tetrahydro-2H-pyran-4-ylmethoxy)pentyl]-1-deoxyribofuranosyl-1-deoxyuridine (57):**

Bromide 46 (0.29 mmol) was subjected to the general procedure D with 1-deoxyribofuranosyl (0.20 mmol) to provide 57 (35 mg, 0.10 mmol, yield 50%). $^1$H NMR (400 MHz, MeOD) $\delta$ 4.14 (d, $J = 12.5$ Hz, 1H, H-6a), 3.92 (dd, $J = 11.8$, 2.6 Hz, 1H, H-6b), 3.99 – 3.94 (m, 2H, H-9a, H-10'a), 3.70 (ddd, $J = 11.2$, 9.3, 4.9 Hz, 1H, H-2), 3.62 (dd, $J = 10.4$, 9.2 Hz, 1H, H-4), 3.49 (t, $J = 6.2$ Hz, 2H, H-2'), 3.48 – 3.35 (m, 5H, H-9'b, H-10'b, H-1'a, H-1'a, H-3), 3.31 (dd, $J = 6.4$ Hz, 2H, H-2'), 3.23 (ddd, $J = 12.1$, 5.3 Hz, 1H, H-1'b), 3.06 (ddd, $J = 10.3$, 2.7 Hz, 1H, H-5), 3.01 (t, $J = 11.7$ Hz, 1H, H-1b), 1.92 – 1.84 (m, 1H, H-7'), 1.84 – 1.72 (m, 2H, H-2'), 1.72 – 1.62 (m, 4H, H-2', H-8a, H-11a), 1.57 – 1.45 (m, 2H, H-3'), 1.34 – 1.32 (m, 2H, H-8'b, H-11'b). $^{13}$C NMR (100 MHz, MeOD) $\delta$ 76.8 (C-3), 75.5 (C-6), 70.2 (C-5'), 67.3 (C-9', C-10'), 67.3 (C-4), 66.4 (C-2), 66.0 (C-5), 53.5 (C-6), 53.4 (C-1), 52.8 (C-1'), 35.2 (C-7'), 29.6 (C-8', C-11'), 28.7 (C-4'), 23.1 (C-3'), 22.5 (C-2'). $[\alpha]^{20}_D = -4.01$ (c = 0.70, MeOH). IR/cm$^{-1}$: 3333, 2923, 2859, 1671, 1433, 1387, 1200, 1136, 1088, 1032. HRMS: found 348.23809 [C$_{16}$H$_{33}$NO$_6$+H]$^+$, calculated for [C$_{16}$H$_{33}$NO$_6$+H]$^+$ 348.23806.

**N-[5-(Thiophen-3-methoxy)pentyl]-1-deoxyribofuranosyl-1-deoxyuridine (58):**

Bromide 47 (0.29 mmol) was subjected to the general procedure D with 1-deoxyribofuranosyl (0.20 mmol) to provide 58 (41 mg, 0.12 mmol, yield 59%). $^1$H NMR (400 MHz, MeOD) $\delta$ 7.41 (dd, $J = 5.0$, 3.0 Hz, 1H, H thio), 7.34 – 7.31 (m, 1H, H thio), 7.10 (dd, $J = 5.0$, 1.2 Hz, 1H, H thio), 4.54 (s, 2H, H-2'), 4.12 (d, $J = 12.2$ Hz, 1H, H-6a), 3.92 (dd, $J = 12.7$, 3.1 Hz, 1H, H-6b), 3.71 (td, $J = 10.1$, 4.5 Hz, 1H, H-2), 3.62 (t, $J = 9.8$ Hz, 1H, H-4), 3.54 (t, $J = 6.2$ Hz, 2H, H-2'), 3.46 (dd, $J = 12.1$, 4.8 Hz, 1H, H-1'a), 3.43 – 3.36 (m, 2H, H-1'a-H-3), 3.21 (td, $J = 12.3$, 5.2 Hz, 1H, H-1'b), 3.11 – 3.02 (m, 1H, H-5), 2.99 (t, $J = 11.7$ Hz, 1H, H-1b), 1.89 – 1.74 (m, 2H, H-2'), 1.69 (ddd, $J = 13.6$, 7.5, 6.0 Hz, 2H, H-2'), 1.53 – 1.45 (m, 2H, H-2'). $^{13}$C NMR (100 MHz, MeOD) $\delta$ 139.5, 127.1, 125.6, 122.6 (C-thio), 76.7 (C-3), 69.3 (C-5'), 67.6 (C-6'), 67.4 (C-4), 66.4 (C-2), 66.0 (C-5), 53.5 (C-6), 53.5 (C-1), 52.9 (C-1'), 28.6 (C-4'), 23.1 (C-3'), 22.5 (C-2'). $[\alpha]^{20}_D = -3.16$ (c = 0.82, MeOH). IR/cm$^{-1}$: 3346, 2963, 2867, 1672, 1429, 1366, 1202, 1133, 1032. HRMS: found 346.16843 [C$_{16}$H$_{27}$NO$_5$S$^+$H]$^+$, calculated for [C$_{16}$H$_{27}$NO$_5$S$^+$H]$^+$ 346.16837.

**N-[5-(Thiophen-3-ethoxy)pentyl]-1-deoxyribofuranosyl-1-deoxyuridine (59):**

Bromide 48 (0.29 mmol) was subjected to the general procedure D with 1-deoxyribofuranosyl (0.20 mmol) to provide 59 (10 mg, 0.028 mmol, yield 14%). $^1$H NMR (400 MHz, MeOD) $\delta$ 7.33 (dd, $J = 5.0$, 2.9 Hz, 1H, H thio), 7.11 (dd, $J = 3.0$, 1.1 Hz, 1H, H thio), 7.02 (dd, $J = 4.9$, 1.3 Hz, 1H, H thio), 4.12 (d, $J = 12.5$ Hz, 1H, H-6a), 3.92 (dd, $J = 12.3$ Hz, 1H, H-6b), 3.74 – 3.70 (m, 1H, H-2), 3.68 (t, $J = 6.7$ Hz, 2H, H-2'), 3.62 (t, $J = 9.7$ Hz, 1H, H-4), 3.52 (t, $J = 6.2$ Hz, 2H, H-2'), 3.45 (dd, $J = 12.1$, 4.8 Hz, 1H, H-1'a), 3.42 – 3.34 (m, 2H, H-3, H-1'a), 3.23 – 3.13 (m, 1H, H-1'b), 3.06 – 3.00 (m, 1H, H-5), 2.97 (t, $J = 11.7$ Hz, 1H, H-1b), 2.91 (dd, $J = 7.1$, 6.3 Hz, 2H, H-2'), 1.86 – 1.70 (m, 2H, H-2'), 1.70 – 1.62 (m, 2H, H-2'), 1.52 – 1.40 (m, 2H, H-2'). $^{13}$C NMR (100 MHz, MeOD) $\delta$ 139.3, 128.1, 124.7, 120.7 (C thio), 76.8 (C-3), 70.8 (C-6'), 69.9 (C-5'), 67.5 (C-4), 66.4 (C-2), 66.0 (C-5), 53.4 (C-1), 53.0 (C-1'), 30.2 (C-7'), 28.7 (C-4'), 24.0 (C-3').
23.1 (C-2'). [α]20D = -9.09 (c = 0.20, MeOH). IR/cm⁻¹: 3358, 3018, 2943, 2870, 1736, 1677, 1439, 1366, 1205, 1134, 1031. HRMS: found 360.18495 [C17H29NO5S+H]+, calculated for [C17H29NO5S+H]+ 360.18392.

**N-[5-(3,3-Dimethyl-1-propyloxy)pentyl]-1-ido-1-deoxynojirimycin (5):**

Bromide 66 (0.30 mmol) was subjected to the general procedure D with 1-ido-1-deoxynojirimycin (0.20 mmol) to provide 5 (16 mg, 0.049 mmol, yield 40%). 1H NMR (400 MHz, MeOD) δ 4.05 (br s, 1H, H-3), 4.03 – 3.94 (m, 3H, H2-6, H-2), 3.71 – 3.64 (m, 1H, H-4), 3.56 (t, J = 7.0 Hz, 1H, H-5), 3.43 (t, J = 6.3 Hz, 1H, H-2'), 3.27 – 3.18 (m, 2H, H-5'), 3.10 – 2.87 (m, 4H, H2-1, H2-1'), 1.82 – 1.53 (m, 2H, H2-2, H2-4'), 1.51 – 1.37 (m, 4H, H2-3), 0.90 (s, 9H, H3-8', H3-9', H3-10'). 13C NMR (100 MHz, MeOD) δ 82.4 (C-6'), 72.4 (C-3), 72.3 (C-5'), 70.3 (C-4), 64.0 (C-2), 55.8 (C-6), 55.3 (C-1'), 53.3 (C-1), 32.9 (C-7'), 30.4 (C-4'), 26.7 (C-8', C-9', C-10'), 24.8 (C-2'), 13.3 (C-3'). IR/cm⁻¹: 3369, 2935, 2860, 1066. HRMS: found 320.2431 [C16H33NO5+H]+, calculated for [C16H33NO5+H]+ 320.2432.

**N-[5-(3,3-Dimethyl-2-butoxy)pentyl]-1-ido-1-deoxynojirimycin (60):**

Bromide 39 (0.32 mmol) was subjected to the general procedure D with 1-ido-1-deoxynojirimycin (0.20 mmol) to provide 60 (14 mg, 0.042 mmol, yield 21%). 1H NMR (400 MHz, MeOD) δ 4.05 (br s, 1H, H-3), 4.03 – 3.95 (m, 3H, H2-6, H-2), 3.93 – 3.86 (m, 1H, H-4), 3.64 (ddd, J = 8.9, 7.6, 4.7 Hz, 1H, H-5'), 3.58 – 3.47 (m, 2H, H-1a, H-5), 3.41 – 3.33 (m, 4H, H1-1'), 3.04 (q, J = 6.3 Hz, 1H, H-6'), 1.95 – 1.72 (m, 2H, H2-2'), 1.66 (dt, J = 12.9, 6.2 Hz, 2H, H-4'), 1.56 – 1.44 (m, 2H, H2-3'), 1.08 (d, J = 6.4 Hz, 3H, H3-7'), 0.91 (s, 9H, H3-9', H3-10', H3-11'). 13C NMR (100 MHz, MeOD) δ 83.3 (C-6'), 70.9 (C-3), 68.9 (C-5'), 67.5 (C-2), 66.4 (C-4), 62.4 (C-5), 60.0 (C-6), 53.7 (C-1'), 53.0 (C-1), 34.6 (C-8'), 29.4 (C-4'), 25.0 (C-9', C-10', C-11'), 23.3 (C-3'), 22.0 (C-2'), 12.8 (C-7'). IR/cm⁻¹: 3372, 2972, 1673, 1393, 1203, 1139, 1066. [α]20D = +1.44 (c = 0.28, MeOH). HRMS: found 334.25937 [C17H35NO5+H]+, calculated for [C17H35NO5+H]+ 334.25880.

**N-[5-(Cyclopentylmethoxy)pentyl]-1-ido-1-deoxynojirimycin (61):**

Bromide 43 (0.30 mmol) was subjected to the general procedure D with 1-ido-1-deoxynojirimycin (0.20 mmol) to provide 61 (23 mg, 0.069 mmol, yield 35%). 1H NMR (400 MHz, MeOD) δ 4.05 (br s, 1H, H-3), 4.03 – 3.94 (m, 3H, H2-6, H-2), 3.90 (br s, 1H, H-4), 3.60 – 3.51 (m, 2H, H-1a, H-5), 3.49 (t, J = 6.3 Hz, H-5'), 3.40 – 3.33 (m, 5H, H1-1b, H2-1', H-2'), 2.17 (dt, J = 14.9, 7.6 Hz, 1H, H-7'), 1.96 – 1.72 (m, 4H, H2-2', H-8'a, H-11'a), 1.71 – 1.54 (m, 6H, H2-9', H2-10', H2-4'), 1.48 (p, J = 7.7 Hz, 2H, H2-3'), 1.34 – 1.25 (m, 2H, H2-11'). 13C NMR (100 MHz, MeOD) δ 75.3 (C-6'), 70.9 (C-3), 70.2 (C-5'), 67.5 (C-2), 66.6 (C-4), 62.4 (C-5), 60.0 (C-6), 53.6 (C-1), 53.0 (C-1'), 39.3 (C-7'), 29.2 (C-8', C-11'), 28.7 (C-9', C-10'), 25.0 (C-4'), 23.1 (C-3'), 21.9 (C-2'). IR/cm⁻¹: 3374, 2953, 2873, 1678, 1440, 1205, 1136, 1072. [α]20D = +4.33 (c = 0.46, MeOH). HRMS: found 332.24355 [C17H33NO5+H]+, calculated for [C17H33NO5+H]+ 332.24315.

**N-[5-(R/S-Tetrahydrofuran-3-ylmethyl)pentyl]-1-ido-1-deoxynojirimycin (62):**

Bromide 44 (0.29 mmol) was subjected to the general procedure D with 1-ido-1-deoxynojirimycin (0.20 mmol) to provide 62 (20 mg, 0.060 mmol, yield 30%). 1H NMR (400 MHz, MeOD) δ 4.08 – 3.95 (m, 4H, H2-6, H-3, H-2), 3.90 (t, J = 3.0 Hz, 1H, H-7), 3.88 – 3.80 (m, 2H, H-9'a, H-10'a), 3.77 – 3.70
(m, 1H, H-9'b), 3.58 (dd, J = 8.6, 5.5 Hz, 1H, H-10'b), 3.56 – 3.52 (m, 2H, H-5, H-1a), 3.50 (td, J = 6.3, 1.8 Hz, 2H, H-5'), 3.44 (dd, J = 9.3, 6.2 Hz, 1H, H-6'), 3.41 – 3.32 (m, 4H, H-1b, H-2', H-6'b), 2.59 – 2.49 (m, 1H, H-7'), 2.09 – 1.99 (m, 2H, H-8'), 1.97 – 1.72 (m, 2H, H-2'), 1.71 – 1.60 (m, 2H, H-2'-4'), 1.48 (p, J = 7.6 Hz, 2H, H-2'). 13C NMR (100 MHz, MeOD) δ 72.5 (C-6'), 70.9 (C-3), 70.5 (C-10'), 70.3 (C-5'), 67.5 (C-2), 67.3 (C-9'), 66.7 (C-4), 62.4 (C-5), 60.0 (C-6), 53.7 (C-1'), 53.0 (C-1), 39.0 (C-7'), 28.7 (C-4'), 28.5 (C-8'), 23.1 (C-3'), 21.9 (C-2'). IR/cm⁻¹: 3355, 2971, 1674, 1201, 1132, 1066. [α]20D = +10.50 (c = 0.40, MeOH). HRMS: found 334.2229 [C₁₆H₁₄NO₆H]⁺, calculated for [C₁₆H₁₄NO₆H]⁺ 334.2224.

**N-[5-(R/S-Tetrahydrofuran-1-ylmethyl)pentyl]-l-ido-1-deoxyojirimycin (63):**

Bromide 45 (0.29 mmol) was subjected to the general procedure D with l-ido-1-deoxyojirimycin (0.20 mmol) to provide 63 (23 mg, 0.069 mmol, yield 34%). 1H NMR (400 MHz, MeOD) δ 4.12 – 3.94 (m, 5H, H-3, H-7', H-2, H-6), 3.93 – 3.83 (m, 2H, H-4, H-10'a), 3.82 – 3.74 (m, 1H, H-10'b), 3.58 – 3.48 (m, 5H, H-1a, H-5, H-5', H-6'a), 3.48 – 3.29 (m, 3H, H-1b, H-2', 1.08 – 1.85 (m, 4H, H-8'a, H-2', H-2'a), 1.85 – 1.73 (m, 1H, H-2'b), 1.70 – 1.59 (m, 3H, H-2', H-8'b), 1.50 (q, J = 7.5 Hz, 2H, H-3''). 13C NMR (100 MHz, MeOD) δ 78.0 (C-3), 73.1 (C-6), 70.9 (C-7'), 70.6 (C-5'), 67.8 (C-10'), 67.6 (C-2), 66.7 (C-4), 62.4 (C-5), 59.9 (C-6), 53.7 (C-1'), 53.0 (C-1), 29.6 (C-4'), 27.5 (C-8'), 25.2 (C-9), 23.1 (C-3'), 21.8 (C-2'). IR/cm⁻¹: 3346, 2871, 1673, 1432, 1200, 1132, 1071. [α]20D = +12.5 (c = 0.46, MeOH). HRMS: found 334.2228 [C₁₆H₁₄NO₆H]⁺, calculated for [C₁₆H₁₄NO₆H]⁺ 334.2224.

**N-[5-(Thiophen-3-methoxy)pentyl]-l-ido-1-deoxyojirimycin (64):**

Bromide 47 (0.29 mmol) was subjected to the general procedure D with l-ido-1-deoxyojirimycin (0.20 mmol) to provide 64 (14 mg, 0.042 mmol, yield 21%). 1H NMR (400 MHz, MeOD) δ 4.54 (d, J = 0.7 Hz, 2H, H-2'), 4.04 (br s, 1H, H-3), 4.01 – 3.93 (m, 3H, H-2-6, H-2), 3.89 (t, J = 3.7 Hz, 1H, H-4), 3.54 (t, J = 6.2 Hz, 2H, H-2'), 3.55 – 3.44 (m, 2H, H-1a, H-5), 3.39 – 3.28 (m, 3H, H-1b, H-2'), 1.98 – 1.72 (m, 2H, H-2'), 1.69 (dt, J = 8.3, 6.3 Hz, 2H, H-2'), 1.50 (q, J = 7.6 Hz, 2H, H-2'), 1.49 (q, J = 7.7 Hz, 2H, H-2'). 13C NMR (100 MHz, MeOD) δ 139.5 (Cq thio), 127.1, 125.6, 122.6 (CH thio), 70.9 (C-3), 69.3 (C-5'), 67.6 (C-6'), 67.5 (C-2), 66.6 (C-4), 62.4 (C-5), 60.0 (C-6), 53.6 (C-1'), 53.0 (C-1), 28.7 (C-4'), 23.1 (C-2), 21.8 (C-3). IR/cm⁻¹: 3346, 2970, 1673, 1409, 1201, 1133, 1066. [α]20D = +8.28 (c = 0.29, MeOH). HRMS: found 346.16823 [C₁₆H₂₇NO₅S +H]⁺, calculated for [C₁₆H₂₇NO₅S +H]⁺ 346.16827.

**N-[5-(Thiophen-3-ethoxy)pentyl]-l-ido-1-deoxyojirimycin (65):**

Bromide 48 (0.29 mmol) was subjected to the general procedure D with l-ido-1-deoxyojirimycin (0.20 mmol) to provide 65 (36 mg, 0.099 mmol, yield 49%). 1H NMR (400 MHz, MeOD) δ 7.33 (dd, J = 4.9, 3.0 Hz, 2H, H thio), 7.14 – 7.09 (m, 1H, H thio), 7.02 (dd, J = 4.9, 1.3 Hz, 1H, H thio), 4.05 (br s, 1H, H-3), 4.01 – 3.95 (m, 3H, H-2, H-2'), 3.90 (t, J = 3.7 Hz, 1H, H-4), 3.68 (t, J = 6.7 Hz, 2H, H-2'), 3.56 – 3.47 (m, 2H, H-1a, H-5), 3.52 (t, J = 6.2 Hz, 2H, H-2'), 3.38 – 3.28 (m, 3H, H-1b, H-2'), 2.94 – 2.88 (m, 2H, H-2'), 1.93 – 1.70 (m, 2H, H-2'), 1.70 – 1.64 (m, 2H, H-2'), 1.53 – 1.37 (m, 2H, H-2'). 13C NMR (100 MHz, MeOD) δ 139.3 (Cq thio), 128.1, 124.7, 120.7 (CH thio), 70.9 (C-3), 70.8 (C-6'), 70.0 (C-5'), 67.5 (C-2), 66.6 (C-4), 62.4 (C-5), 60.0 (C-6), 53.7 (C-1'), 53.0 (C-1), 30.2 (C-7'), 28.7 (C-4'), 23.1 (C-3'), 21.8 (C-2'). IR/cm⁻¹: 3355, 2971, 1674, 1394, 1202, 1066. [α]20D = +2.52 (c = 0.71, MeOH). HRMS: found 360.18397 [C₁₇H₂₉NO₅S +H]⁺, calculated for [C₁₇H₂₉NO₅S +H]⁺ 360.18392.
References:


